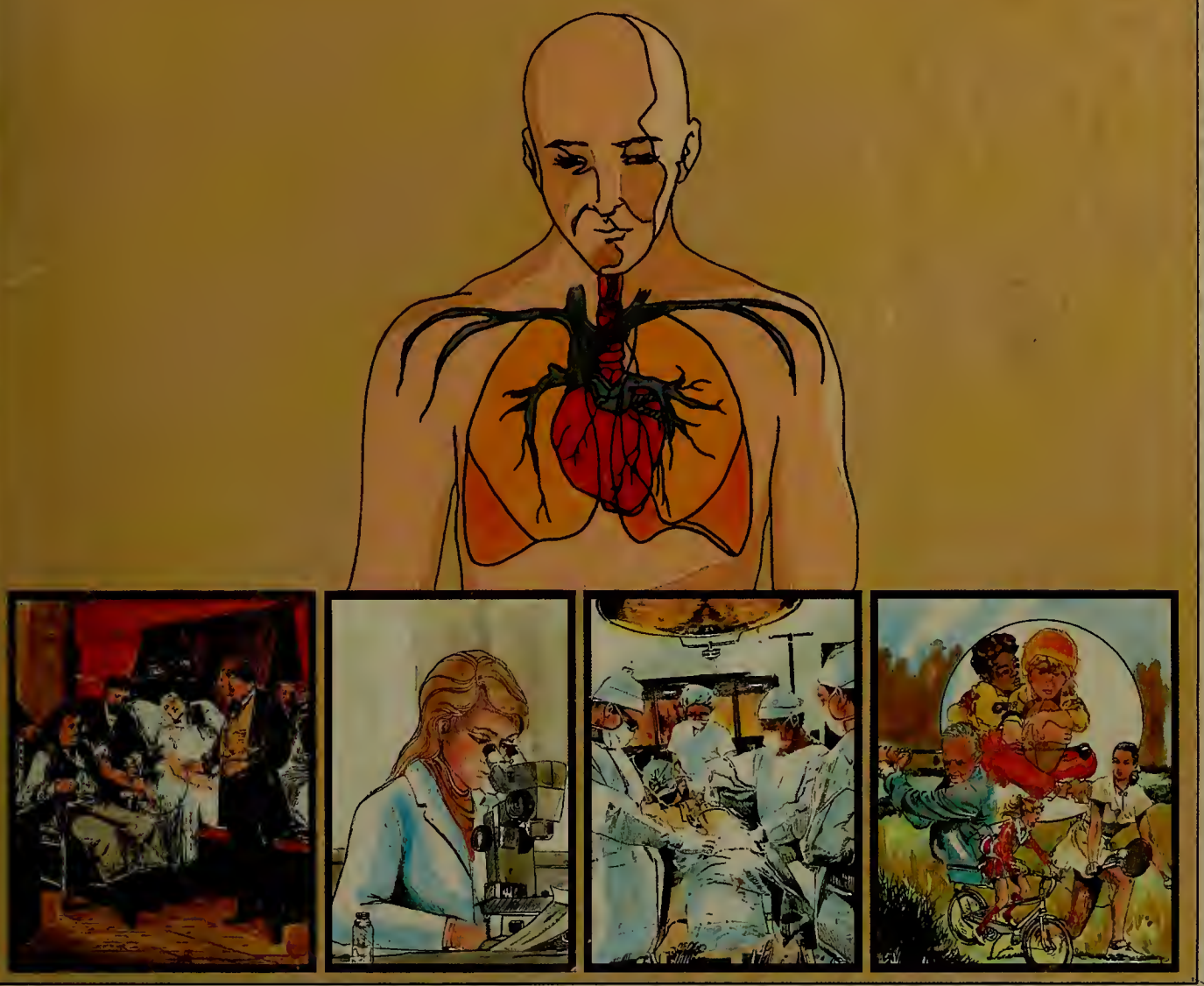
Years of Progress for the People in Heart, Lung, and Blood Diseases

1948-78



The Sixth Report of the National Heart, Lung, and Blood Advisory Council to The President and The Congress of the United States

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service - National Institutes of Health

30 Years of Progress for the People in Heart, Lung, and Blood Diseases

1948-78

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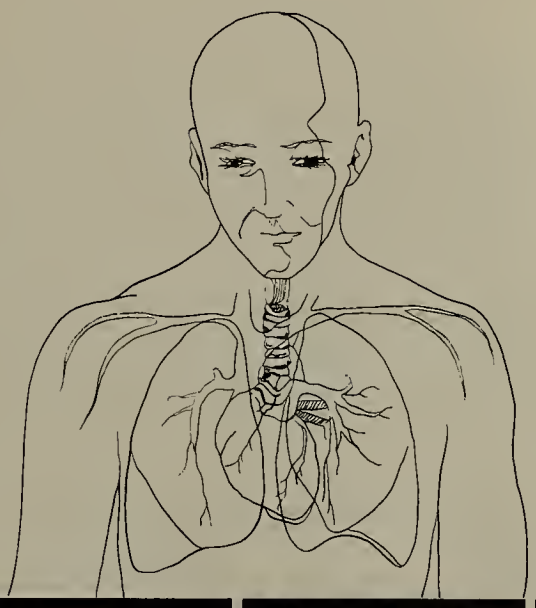

October 9, 1978

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service - National Institutes of Health

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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH
BETHESDA, MARYLAND 20014

NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

October 9, 1978

The President
The White House
Washington, DC 20500

Dear Mr. President:

The members of the National Heart, Lung, and Blood Advisory Council are pleased to submit to you, and to the Congress, our sixth report on the progress of the National Heart, Lung, and Blood Institute's effort to prevent and cure diseases of the heart, blood vessels, lungs, and blood. This report has been prepared in accordance with Public Law 95-83.

In keeping with its charter, the Advisory Council has endeavored to perform its function of review and evaluation of the program and direction of the National Heart, Lung, and Blood Institute with a view to ensuring that the Institute's activities continue to serve the public's best interests.

Our report focuses on progress in heart, lung, and blood diseases since the establishment of the Institute just 30 years ago, and on future needs.

Mr. President, to better fulfill your objectives, those of the Congress, and the needs of the individual American citizen, the Council reaffirms its desire and availability to be of service.

Respectfully,

The National Heart, Lung, and Blood Advisory Council

William P. Baker — James C. Hunt — William D. Mallory
Eugene Braunwald — Thomas N. James — Gilbert S. Omenn
Dorothy L. Brooks — Thomas R. Jones — Alan K. Peirce
Lewis A. Lay — Betty J. Kennedy — Ben W. Pennoy
Harry W. Fritts, Jr. — Ira L. Looney — Richard S. Ross
Lawrence Lowell — Sheryl Guthrie Lycan — Ruth Ross
Millicent Higgins — Caroline D. Lurie — Dallas K. Willman

NATIONAL HEART, LUNG, AND BLOOD ADVISORY COUNCIL

EUGENE BRAUNWALD, M.D.
Harvard Medical School
Peter Bent Brigham Hospital
Boston, Massachusetts

DOROTHY L. BROWN, M.D.
Meharry Medical College
Nashville, Tennessee

BERNARD W. D. FONG, M.D.
1380 Lusitana Street
Honolulu, Hawaii

HARRY W. FRITTS, JR., M.D.
School of Medicine
State University of New York
Stony Brook, New York

GARETH M. GREEN, M.D.
School of Hygiene and Public Health
The Johns Hopkins University
Baltimore, Maryland

MILLICENT W. HIGGINS, M.D., D.P.H.
School of Public Health
University of Michigan
Ann Arbor, Michigan

JAMES C. HUNT, M.D.
College of Medicine
University of Tennessee
Memphis, Tennessee

THOMAS N. JAMES, M.D.
University of Alabama Medical Center
Birmingham, Alabama

THOMAS R. JONES
St. Francis Hospital Medical Center
Peoria, Illinois

BETTY JEAN KENNEDY, M.D.
St. Mary's Hospital
Lewiston, Maine

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KXIV, Inc.
Phoenix, Arizona

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Howard University
Washington, D.C.

CAROLINE LURIE
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New York, New York

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Southwestern Medical School
University of Texas
Dallas, Texas

HELEN M. RANNEY, M.D.
School of Medicine
University of California, San Diego
La Jolla, California

RICHARD S. ROSS, M.D.
School of Medicine
The Johns Hopkins University
Baltimore, Maryland

RUSSELL ROSS, D.D.S., Ph.D.
School of Medicine
University of Washington
Seattle, Washington

VALLEE L. WILLMAN, M.D.
School of Medicine
St. Louis University
St. Louis, Missouri

*ROBERT I. LEVY, M.D. (Chairman)
Director, National Heart, Lung, and Blood Institute
National Institutes of Health
Bethesda, Maryland

EX OFFICIO

WILLIAM P. BAKER, M.D., Ph.D.
National Naval Medical Center
Bethesda, Maryland

*DONALD S. FREDRICKSON, M.D.
Director, National Institutes of Health
Bethesda, Maryland

*JOSEPH A. CALIFANO, JR.
Secretary
Department of Health, Education, and Welfare
Washington, D.C.

WILLIAM F. MALONEY, M.D.
Office of Academic Affairs
Veterans' Administration
Washington, D.C.

GILBERT S. OMENN, M.D., Ph.D.
Office of Science and Technology Policy
Washington, D.C.

*Did not participate in the preparation of this report.

American Heart Month, 1978

By the President of the United States of America

A Proclamation

Diseases of the heart and blood vessels afflict some thirty million Americans. Each year cardiovascular disorders claim nearly one million lives and cost our economy nearly forty-eight billion dollars in lost wages, lost productivity, and medical expenses.

Since 1948, a concerted national effort has been under way to reduce illness, disability, and death from heart and blood vessel diseases through nationwide programs of biomedical research in the cardiovascular field, training of research workers and clinicians, information and education programs for health professionals and for the general public, and community service activities concerned with prevention, detection, and control of cardiovascular disorders.

These efforts have been spearheaded by the National Heart, Lung, and Blood Institute, a federal agency, and the American Heart Association, a voluntary health organization supported through private contributions. Since 1948, their combined outlay in support of the national battle against cardiovascular diseases has totaled nearly three billion dollars.

During these thirty years, an immense amount of new knowledge about the cardiovascular system and its diseases has been amassed and much of it has found application in better methods of prevention, diagnosis, and treatment. In addition, many Americans have modified their diets, established sensible and regular exercise programs, changed their smoking habits, or have otherwise altered their lifestyles to achieve better cardiovascular health. As a result, mortality rates have declined steadily since 1950 in nearly all major cardiovascular disease categories and the total number of deaths among Americans from these diseases is the lowest it has been since 1965.

But these encouraging results are no excuse for complacency. On the contrary, they show that it is only through sustained dedication and cooperation among public officials, community leaders, private institutions, and the American people that we have any chance of controlling this threat to the health of our Nation.

Recognizing the need for all Americans to join forces in the battle against cardiovascular disease, the Congress, by joint resolution approved December 30, 1963 (77 Stat. 843; 36 U.S.C. 169b) has requested the President to issue annually a proclamation designating February as American Heart Month.

NOW, THEREFORE, I, JIMMY CARTER, President of the United States of America, do hereby proclaim the month of February, 1978, as American Heart Month. I invite the Governors of the States, the appropriate officials of all other areas subject to the jurisdiction of the United States and the American people to join with me in reaffirming our commitment to the search for new ways to prevent, detect and control cardiovascular disease in all its forms.

IN WITNESS WHEREOF, I have hereunto set my hand this nineteenth day of January, in the year of our Lord nineteen hundred seventy-eight, and of the Independence of the United States of America the two hundred and second.

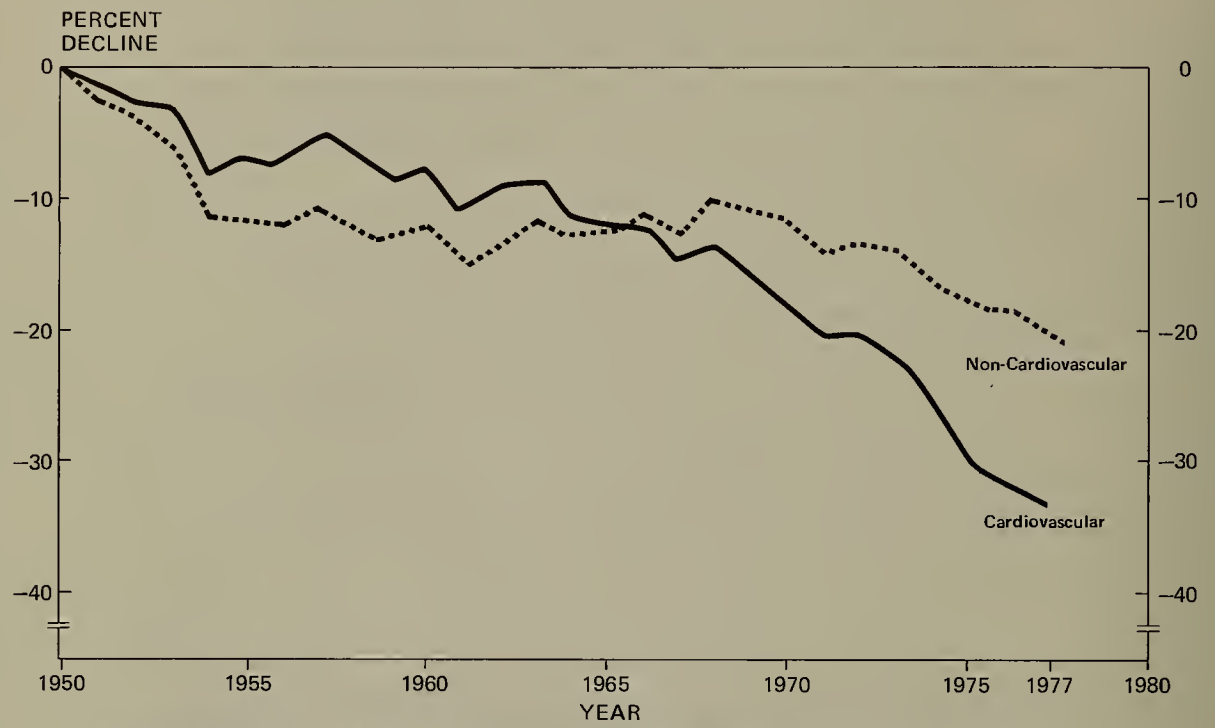
Jimmy Carter

CONTENTS

A BRIEF INFORMAL GLOSSARY

Needlessly complex terminology has been avoided in this report. For easier reading, however, at the back of this report are brief clarifications of some recurrent key technical terms that may not be explained in the text.

Figure 1. *Decline in Death Rates for Cardiovascular and Non-Cardiovascular Diseases, U.S., 1950-1977.*



Death rate is age-adjusted to U.S. Population, 1940. Rate for Cardiovascular Diseases (CVD) excludes congenital heart disease.

Source: National Heart, Lung, and Blood Institute from data from the National Center for Health Statistics.

DEATHS PER 100,000 POPULATION			
Year	CVD	Non-CVD	Total, All Causes
1950	425.6	415.9	841.5
1977	282.5	335.6	618.1
Change	−143.1	− 80.3	−223.4
% Change	− 33.6	− 19.3	− 26.5

AS WE SEE IT . . .

SINCE the establishment of the National Heart Institute 30 years ago, the Congress has given the Institute continuous and uninterrupted support and encouragement. During this period there has been an enormous investment of time, effort, talent, and considerable fiscal resources to carry out the Institute's goals and objectives. Its mission has been expanded to include diseases of the lung, blood, and blood vessels.

The 1972 renewal legislation broadened the Institute's mandate. It also required the Institute to develop a clearly defined program listing goals, objectives, and priorities for research, research training, and advancement of activities in prevention and control.

The Institute's program has been highly successful in bringing forth new knowledge that is being translated into improved health care and medical care. The impact of research contributions developed since the Institute was established in 1948 is reflected in decreased mortality and morbidity from heart diseases. It is seen most dramatically in the sharp decrease in cardiovascular deaths since 1950 (figure 1).

This report represents an effort to outline some of these contributions in the context of a brief historical perspective against which readers can evaluate the significance of these advances to the people of the United States. The report includes the Council's recommendations for the future and its budgetary recommendations for the National Heart, Lung, and Blood Institute (NHLBI) for Fiscal Years 1980 through 1983.

—National Heart, Lung, and Blood
Advisory Council

THE NATIONAL HEART, LUNG, AND BLOOD INSTITUTE

FAR more progress has been made in the control, cure, and prevention of diseases of the heart, lungs, blood, and blood vessels during the past 30 years than in the entire span of human history before 1948. This explosion of medical research, knowledge, and application has had an enormous impact on health and longevity.

It is no coincidence that enormous progress in biomedical science has occurred during the 30-year existence of the NHLBI. Many circumstances and developments have contributed to this progress, but there is no doubt that the central mobilizing factor has been the Institute's impetus, encouragement, and financial support of basic and applied research, as well as its focus on the continuum from the laboratory bench to the patient's bedside.

In heart disease alone, today's medical and health care realities have far outstripped any reasonable expectations of the Congress and the public in 1948, when President Harry S. Truman signed the act that created the National Heart Institute. The Institute began with a Congressional mandate of primary responsibility for Federal research and training programs in cardiovascular diseases. This mandate has since been broadened by the Congress to include lung diseases (in 1969) and blood diseases and blood resources (in 1972).

To carry out its mission, the NHLBI receives operating funds each year from the Congress. Annual funding has increased from $16 million in FY 1950, the first year of appropriations, to approximately $448 million in FY 1978. Monies allocated to the Institute support extramural programs of research grants, research and development contracts, and research training programs; public and community-oriented demonstration programs and educational and prevention activities; and other programmatic activities nationally and internationally, as well as intramural research programs and day-to-day administrative operations.

The NHLBI's main function is to serve as a center for a large, broadly based, and diversified support program against cardiovascular, pulmonary, and blood disorders. Planning for research, training, education, and prevention programs is a long, complex, and continuous process that must always be focused on the future. The process involves painstaking deliberations among numerous expert consultants, the Institute's staff, the National Heart, Lung, and Blood Advisory Council, various technical advisory committees, and the Director of the NHLBI, conducted on a schedule that permits resource commitments several years in advance.

The Institute's mission includes some of mankind's oldest afflictions, diseases that have significantly shortened life with little effective challenge. Heart, lung, and blood diseases have long been recognized. Evidence of blood vessel lesions has been found in Egyptian mummies. From the days of the pharaohs to the early 1900's, life expectancy for adults changed little, and in some countries it was less than 30 years.

In all areas of heart, lung, and blood diseases, striking changes have occurred during the 30-year existence of the NHLBI. Deaths from heart attack, stroke, rheumatic fever, valvular heart disease, pneumonia, tuberculosis, hemophilia, and pernicious anemia—to name only a few—have declined markedly as a result of improved sanitation, better nutrition, new drugs, scientific discoveries, new information provided by biomedical researchers, improved medical and professional education, and increased access to better medical care.

Our expanded knowledge has resulted in part from research supported by the NHLBI. However, many diseases continue to challenge the Institute and the scientists who carry out its programs. Among these are atherosclerosis, heart attack, hypertension, stroke, diabetes, chronic obstructive lung disease, cystic fibrosis, and sickle cell anemia. These and other chronic problems provide fruitful areas now and in the future for research aimed at improving health, quality of life, and life expectancy.

The Institute is prepared to meet these challenges with boldness and imagination. With the assistance and strong support of the National Heart, Lung, and Blood Advisory Council, the Institute is actively involved in developing new and expanded research and training missions to prepare generations of young scientists to carry out its programs.

THE NATIONAL HEART, LUNG, AND BLOOD ADVISORY COUNCIL

THE National Advisory Council's involvement in the affairs and programs of the NHLBI began when the Institute was initiated, for the National Heart Act of 1948 also created the Council. Its first executive director was Dr. Paul Dudley White, who also served the Institute as voluntary chief medical advisor.

From the very beginning, the Council has strongly advocated a balanced program of research, research training, and education—initially in cardiovascular diseases and subsequently also in lung and blood diseases and blood resources as the Institute's mission expanded. During its early years, the Advisory Council itself reviewed in detail all research grant applications. However, with the remarkable growth of the Institute's extramural research programs, it became necessary to rely on study sections and special review groups for initial review, with the Council providing final review. The Council today remains keenly attentive to individual investigators and their research proposals, and endeavors to ensure that high-quality, creative research in the public interest continues to be supported.

The National Heart Act required the National Advisory Heart Council to be broadly representative. The Act provided for inclusion of fundamental scientists, medical practitioners in cardiovascular diseases, residents in training, and ex officio members from the Public Health Service, the Veterans' Administration, the Army, and the Navy. In addition, provision was made for representatives of the lay public who had a special interest in medical affairs. So constituted, the Council has served as a cross-sectional national group committed to the public interest and well suited for its leadership responsibility.

When the National Heart, Blood Vessel, Lung, and Blood Act of 1972 expanded the functions and responsibilities of the Institute, it also enlarged the Council's membership (from 16 to 23 members) and

Figure 2. *An early National Advisory Heart Council meeting in 1949.*

its scope. In addition to providing counsel and assistance in the funding of extramural research activities, the Council now provides advice on virtually every aspect of the Institute's programs. Research and funding strategies are important items on the Council's agenda. Although the Council does not review individual research contract proposals, it does review the overall boundaries and scope of research activities supported by these contracts. It is the only such advisory council that reviews concepts in new contract initiatives and the percentage of research funds spent on contracts.

Over the years, the Council has provided leadership and initiative in many areas. Among these are training of young research scientists, construction of research facilities, support of demonstration and disease control programs, development of joint programs with other institutes of NIH, development of cooperative research units at extramural institutions prior to completion of the Institute's own research facilities, promotion of cooperative research exchanges with foreign countries, establishment of field studies and clinical trials, provision of long-term stable support to productive programs of research and research training, recognition and refinement of ethical standards in research involving human subjects, and development of improved information and educational systems and services for the public and the medical profession.

Since its inception in 1948, the Advisory Council has had a total of 118 appointed members. Appointment is usually for a single term of 4 years and entails a commitment of much time and effort each year. In addition to appointed members, some 30 representatives of Federal agencies have served as ex officio members since the Council's first meeting. The 30th anniversary of the Institute was celebrated with special recognition of Mrs. Albert D. Lasker's contributions. She was the recipient of the Council's first Distinguished Service Award.

As required by law, the National Heart, Lung, and Blood Advisory Council each year submits its own report to the President and the Congress on the Institute's progress toward achievement of its goals. This report for 1978 has been prepared in compliance with that requirement.

Figure 3. *Mrs. Albert D. Lasker was honored by the Council at a special celebration of the 30th anniversary of the National Heart, Lung, and Blood Institute in 1978.*

PROGRESS IN HEART, LUNG, BLOOD, AND BLOOD VESSEL DISEASES

JUST as the improved health care of today is based on the cumulative biomedical research achievements of past years, so will the research accomplishments of today make possible the health care advances of tomorrow.

Contrary to popular conception, such progress in the biological sciences seldom occurs through major independent discoveries or spectacular breakthroughs. Rather, research goals are almost invariably attained by steady, painstaking and usually slow accumulation of knowledge—bit by bit—until some fragment of information fills a crucial gap in the biomedical jigsaw puzzle and thus shows the way to a major advance, and sometimes to a long succession of major advances.

During the past 30 years, great progress has been made in the detection, evaluation, and management of diseases of the heart, lung, blood, and blood vessels, and in our ability to use blood as a lifesaving medical resource. Using a question-and-answer editorial format, the Council has selected a few of these advances, as well as areas of continuing challenge, to best illustrate this progress.

Figure 4. *An aneurysm of the abdominal aorta has been surgically replaced with a graft. Dr. Michael DeBakey, who pioneered this work 25 years ago, used a graft made of Dacron cloth in the early days (as shown). Research and testing of a wide range of possible biomaterials have led to increased patency of such grafts and improved nonreactivity with surrounding tissues. Today, the grafts are fabricated from special Dacron.*

HEART AND BLOOD VESSEL DISEASES

PERHAPS the most spectacular and rapid medical progress of the past 30 years has been that made in understanding the causes, mechanisms, and management of a number of common cardiovascular diseases.

Radical changes in understanding and managing *heart attacks* have achieved a striking reduction in the death rate, and the hospital stay following a heart attack has been markedly shortened.

The prevalence of *rheumatic fever* has been greatly reduced, sparing millions of people permanent heart valve damage associated with this disease. However, streptococcal infection and rheumatic fever still damage the hearts of thousands of children and some adults every year. Artificial heart valves are restoring health to many of these victims.

Congenital lesions of the heart, essentially untreatable 30 years ago, can now usually be corrected by surgery. Blood vessel disease that results in obstruction or leakage can now, in many instances, be treated by substituting other vessels or artificial vessels.

Most bacterial infections of the heart valves used to be uniformly fatal. They can now generally be cured without serious lasting damage. However, other causes of common abnormalities of the heart valves and muscle, known as *cardiomyopathies*, continue to exact a heavy toll. Important advances have been made in detection and diagnosis; however, before successful treatment is possible, much more research is needed.

For the growing number of people with *diabetes,* insulin and oral hypoglycemic drugs afford a relatively normal life; but the disease continues to damage every body system, and the life span is likely to be cut short by severe complications, mostly cardiovascular. Institute-supported research, aimed at eliminating complications of diabetes, is focused primarily on understanding how the disease accelerates atherosclerosis, and how it produces other pathologic cardiovascular effects.

ATHEROSCLEROSIS AND HEART ATTACK

THE term heart attack is a lay expression for acute myocardial infarction. Myocardial infarction literally means "death of heart muscle," and this anatomic feature has been recognized by pathologists for several hundred years. By 1910 heart disease had become the leading cause of death in the United States. Yet heart attack was not recognized as a clinical entity until 1912. Before then the acute, crushing chest pain that is now recognized as the hallmark of a heart attack was thought to be associated more with an intestinal problem than with a cardiovascular event. It was thought that the victims died of "indigestion."

Why have heart attack and coronary heart disease received so much lay and professional attention in recent years?

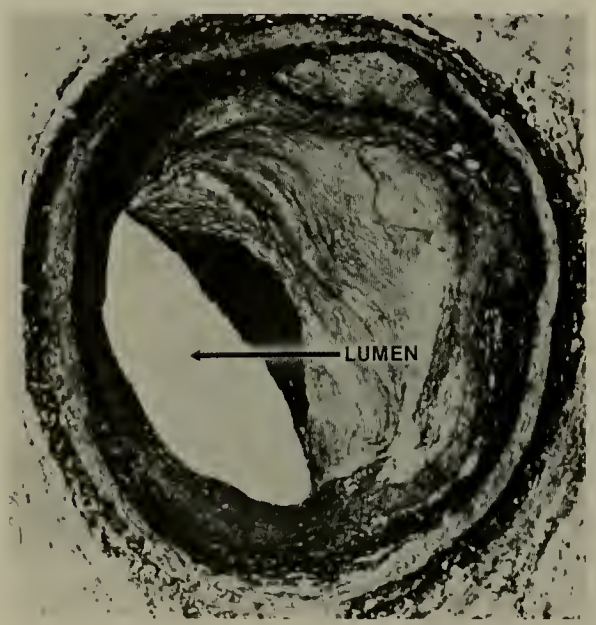
Heart attack occurs in approximately 1,250,000 Americans annually, and more than 600,000 persons die from this condition each year. Heart attack is the single most common cause of death in this country, and in virtually all instances it results from the atherosclerotic process. Thus coronary heart disease accounts for chronic illness in more than 4 million adult Americans and ranks number one as a cause of disability. Some years ago the National Heart, Lung, and Blood Institute saw this as a problem of virtually epidemic significance and sounded a nationwide alarm.

What is atherosclerosis? Is it the same thing as arteriosclerosis?

They are often confused, but they are not the same. Arteriosclerosis is commonly called hardening of the arteries, and it covers a variety of conditions that cause the arterial walls to become thick and hard. Atherosclerosis is a form of arteriosclerosis in which the inner layer of the artery wall is made thick and irregular by an increase in the number of cells in this layer, accompanied by formation of new tissue and by deposits of fatty substances and other materials. These lesions are known as atherosclerotic

plaques (see figure 5). As they build up on the inner surface of the artery, they reduce the inside diameter and may eventually impede or obstruct the flow of blood. When this occurs in the coronary arteries that supply the heart muscle, it leads to coronary artery disease and to heart attack.

Figure 5. *A cross section of an arteriosclerotic vessel showing typical thickening of the walls and consequent diminution in the size of the lumen through which the blood travels. A normal artery would have a larger circular lumen.*



Is the answer to the heart attack problem primarily one of curing and preventing atherosclerosis?

Yes. However, the cause of atherosclerosis is still much debated, and the eradication of this problem may take many years. It is important for the medical and lay public, therefore, to seek all possible means of improving the survival rate of heart attack victims, while researchers simultaneously seek a better understanding of its cause and an appropriate approach to its prevention.

What causes death in victims of heart attack?

A variety of causes has been identified. In a significant number of victims, death results from an abnormal heart rhythm that culminates in sudden cardiac arrest. In many others, death is caused by occlusion of one of the large coronary arteries. This seriously reduces the supply of oxygen to the heart muscle, causing some of the muscle to lose function and die. A major attack, with death of a large segment of heart muscle, may bring on acute heart failure and death. In still other victims, recurrent and progressive heart attacks, although milder, cause a more gradual loss of functioning heart tissue and commonly result in chronic heart failure, progressive disability, and death.

Has the death rate from heart attack decreased since the National Heart, Lung, and Blood Institute sounded the nationwide warning mentioned earlier?

Yes, spectacularly. Death rates have decreased significantly for men aged 45 to 54. However, this has not occurred in European countries, with the exception of Finland, as table 1 illustrates. The decline in death rates for men aged 55 to 64 is also greater in the United States (see table 2). The majority of acute deaths following a heart attack occur before the person can be admitted to the hospital, or soon after admission. In recent years, a striking decrease in the death rate has been achieved by improved hospital care with the advent of intensive coronary care units. *Not only has early mortality decreased, but the hospital stay for the heart attack victim has also been markedly shortened and the cost of care thereby reduced.* The hospital stay has been shortened from 6 weeks, 20 years ago, to 10 days today—and certain selected low-risk patients can safely be discharged after as little as 1 week.

Now that the heart attack problem is recognized earlier and more commonly, have there been major changes in treatment?

Radical changes. Thirty years ago the standard treatment was to place the patient at bed rest for 6 weeks, in the belief that the heart should be "splinted," like a broken bone, and spared any unnecessary workload. Many persons became cardiac cripples as a result of the unnecessarily prolonged hospitalization. In the 1960's some physicians tried letting the heart attack patient walk around earlier. The workload on the heart was not significantly increased by having the person first sit, then stand and walk; with such assurance that total disability need not occur, the patient was much less likely to develop

Table 1. *Change in Death Rates for *Coronary Heart Disease, Selected Countries, 1969-73 (Men, Aged 45-54).*

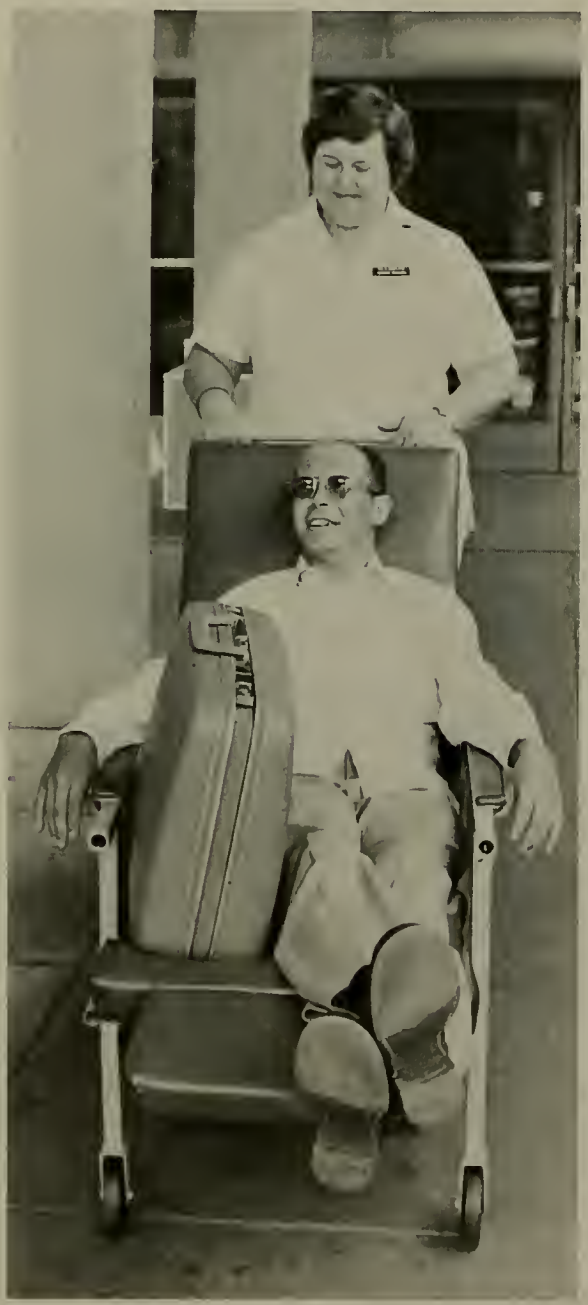
COUNTRY	CHANGE 1969-73	DEATHS PER 100,000 POPULATION 1969	1973
United States (white)	−28.3	341.2	312.9
Finland	−17.1	427.3	410.2
Austria	− 0.4	146.7	146.3
Italy	+ 0.6	112.9	113.5
Netherlands	+ 2.5	188.8	191.3
Switzerland	+ 4.1	103.4	107.5
German Fed. Rep.	+ 9.3	146.4	155.7
Hungary	+21.5	142.8	164.3
Sweden	+30.1	126.0	156.1
Norway	+31.1	191.5	222.6
England and Wales	+31.6	254.9	286.5
Denmark	+31.9	159.5	191.4
Northern Ireland	+43.2	318.9	362.1
Scotland	+43.5	329.2	372.7

Table 2. *Change in Death Rates for *Coronary Heart Disease and all Causes, Selected Countries, 1969-74 (Men, Aged 55-64).*

	CORONARY HEART DISEASE		ALL CAUSES	
COUNTRY	DEATHS PER 100,000 1974	% CHANGE 1969-1974	DEATHS PER 100,000 1974	% CHANGE 1969-1974
United States (white)	814.0	−11.5	2026.1	− 8.1
Switzerland	284.8	− 6.0	1558.6	−10.2
Norway	589.8	− 6.0	1537.7	− 5.3
Finland	1007.0	− 2.9	2485.9	− 9.1
Netherlands	509.3	+ 0.3	1663.8	− 3.3
England and Wales	733.6	+ 3.5	2019.3	− 6.7
Scotland	952.0	+ 5.5	2440.0	− 1.4
German Fed. Rep.	491.1	+ 5.8	2015.5	− 7.5
Italy	326.6	+ 6.1	1804.4	− 7.6
Austria	475.9	+ 7.8	2015.5	− 8.3
Denmark	584.9	+ 8.3	1694.0	+ 1.7
Hungary	477.3	+11.4	2125.0	+ 8.1
Sweden	543.4	+11.7	1429.1	− 0.8
Northern Ireland	963.7	+16.1	2347.4	+ 6.7

*In the vast majority of deaths from coronary heart disease, the immediate cause of death is a heart attack.

Figure 6. *This patient is happy to be going home from the hospital only 7 days after he suffered an uncomplicated heart attack. Prior to an NHLBI study of early hospital discharge at Duke University Medical Center, this patient would have remained in the hospital an additional 10 days, incurring an additional cost of approximately $2,000.*



emotional problems. This increased the survival rate because early activity reduced the frequency of other complications, and also because reassurance tended to eliminate the adverse psychological effects of the so-called "postcoronary depression syndrome."

What are some of the more recent research directions to aid victims of heart attack?

Experiments have shown conclusively that the amount of heart muscle in animals that becomes nonfunctional and dies can be reduced by prompt drug treatment *after* a coronary occlusion.

Current research in patients is designed to test how drug therapy can be applied to patients with heart attacks. There is also considerable hope that drugs such as aspirin (which interfere with blood clotting) and beta-blockers (agents that reduce the heart's need for oxygen) will materially improve the long-term survival of heart attack victims. This important question is now being addressed by two clinical trials supported by the NHLBI.

What are the principal reasons for a decrease in mortality from heart attack?

Many factors are involved. First, the frequency of heart attack appears to be decreasing, as the public becomes more aware of the risk factors for atherosclerosis and the importance of changing them. Smoking has been recognized as one of the important risk factors. Obesity, particularly for the person who has symptomatic coronary artery disease, causes increased cardiac workload. High blood pressure is another common and serious risk factor. Increased physical activity, dietary control of cholesterol and saturated fats, cessation of smoking, and control of high blood pressure probably account for much of the reduction in heart attack morbidity and mortality.

Have advances in medical management contributed to this decrease in mortality?

Yes. Cardiac arrhythmias can now be better managed through a number of new developments. These include better techniques of electrocardiographic monitoring; the demonstration of abnormal heart rhythms; the development of antiarrhythmic drugs that can return an abnormal rhythm back to a regular heartbeat and can prevent the reemergence of abnormal rhythms; and the development of cardiac pacemakers to maintain normal

Figure 7. *There is a great contrast in the medical care received by heart attack patients in the past (top) and today (bottom). Whereas patients mainly received bed rest and some drug therapy in the mid-1950's, today a Coronary Care Unit has extensive monitoring and health care capabilities. A highly qualified nurse is seen attending the patient. Drugs can be administered by precision instruments directly into a vein (see apparatus on far left) under the attention of a nurse. Some years ago, drug administration was done only by physicians. This tended to limit the minute-by-minute attention such critically ill patients need. Today, the nurse also helps the physician monitor blood pressure, cardiac output, respiration, and onset of heart fibrillation. These events are continuously monitored with the aid of a multichannel oscilloscope (seen in background) so that instant remedial action, such as defibrillation of the heart, administration of oxygen, or other emergency actions can be taken by the Coronary Care Unit staff when needed.*

Figure 8. *The dietitian is demonstrating plastic models of various foods and discussing their relative portion size and nutritional value with a patient. This is part of the Coronary Primary Prevention Trial. Such dietary counseling is one of many important aspects of work undertaken at the 11 Lipid Research Clinics funded by the NHLBI.*

cardiac electrical activity in persons with persistent rhythm disturbances such as heart block. All of these developments have contributed to the reduction of deaths, particularly during the first few days after a heart attack. Other means of providing temporary assistance to the heart and circulation have also advanced greatly.

What is the current status of coronary artery surgery in management of coronary heart disease?

Studies and experience with coronary artery bypass surgery have not entirely resolved the question of its role. It is clear that most patients with intractable pain associated with angina pectoris can confidently expect improved quality of life with this procedure. Also, persons with major obstruction of the main left coronary artery have an increased chance of survival if a satisfactory bypass operation can be performed. For disease involving other coronary arteries, there is less convincing evidence for improved long-term survival following bypass surgery. Clearly, however, the results of medical and surgical management have improved markedly in the last 30 years, particularly the last decade.

Validation through clinical trials is necessary to compare the usefulness of medical and surgical treatment of coronary artery disease. From the current state of our knowledge, it seems likely that medical and surgical treatment will eventually be used in a cooperative rather than competitive fashion, and that the specific therapy will be tailored to the individual patient. Validation of the desired therapeutic approach (via a clinical trial) is now underway.

Is is possible to reverse the atherosclerotic process?

This question cannot yet be answered in humans; however, in laboratory animals, lowering high blood cholesterol levels through decreased intake of dietary cholesterol and fat appears to cause regression of atherosclerotic plaques. Much additional research is needed in this area, for heart attack cannot be prevented until the atherosclerosis problem is resolved. The Institute is involved in a clinical trial to determine the effect of lowered cholesterol on the progress of atherosclerosis in patients who have had a myocardial infarction.

ARRHYTHMIAS AND SUDDEN CARDIAC DEATH

THERE are several definitions of sudden death. One of the more commonly used is death within 24 hours of the onset of symptoms. It is the kind of death meant by the common expressions that someone has "dropped dead," or has died "during sleep" or "before the doctor could get there." In most cases it is related to the heart, and it may then be termed more specifically sudden cardiac death. More than 450,000 people in the United States alone die this way every year.

What is the cause of sudden cardiac death?

Institute research during the last few years has established that a large majority of persons who die

suddenly have advanced coronary atherosclerosis. Of the more than 640,000 deaths each year from coronary heart disease, more than 385,000—over 60 percent—occur before hospitalization.

The more immediate cause of death in the vast majority of these victims is the development of a type of severe cardiac arrhythmia—called ventricular fibrillation—a disturbance of the heart's electrical activity in which the heart goes out of control and quivers wildly, but does not beat effectively. The heart's pumping action suddenly stops, producing immediate collapse. Unless a more normal rhythm is restored within 2 to 4 minutes, the patient will die within several minutes more.

There are also many other causes: Disturbance of heart rhythm may result from congenital heart defects, valvular heart disease, or heart muscle inflammation. . . . A large blood clot may form in the veins, reach the heart, be pumped into the main artery leading to the lungs, and then obstruct the flow of blood. . . . A clot or hemorrhage may occur in an important artery leading to the brain, or in the brain circulation itself. All these causes of sudden death are under active investigation by the Institute.

If death occurs so quickly, can anything effective be done to save and prolong the lives of these people?

Yes. This was positively demonstrated in the hospital coronary care units early in the 1960's, when prompt resuscitation of patients with ventricular fibrillation first became possible. These people often recovered uneventfully, and their subsequent course of recovery became similar to that of other patients who had recovered from a heart attack. Thousands of these individuals have gone on to live useful, comfortable lives for many years.

What can be done for the sudden death victim who is *not* in the hospital?

First, many of these sudden death victims are actually suffering from heart attacks at the moment of collapse. Prompt cardiopulmonary resuscitation at the scene places them in exactly the same status as patients who have developed ventricular fibrillation in the hospital, especially in coronary care units. Second, many patients who have collapsed suddenly, with or without heart attacks, and have been resuscitated, have returned to satisfactory lives, despite the presence of underlying coronary artery disease.

Is it possible to predict who will be a victim of sudden death?

Absolutely accurate prediction on an individual basis is not yet possible. However, a number of studies have identified groups of patients who are at unusually high risk of sudden death. These include certain survivors of previous episodes of ventricular fibrillation, survivors of heart attack who show continued instability of cardiac rhythm, and people with certain electrocardiographic abnormalities.

What can be done to reduce sudden deaths?

A three-pronged attack is required. First, and most immediately, through community-wide education many people can be trained to carry out effective cardiopulmonary resuscitation and thereby save people who collapse suddenly on the street or in public facilities. Second, as rapidly as possible, we must refine our ability to identify people who are at risk of sudden death, and to determine whether preventive treatment is possible. Such a clinical trial is now underway. Finally, the underlying abnormality in the majority of patients—coronary atherosclerosis—must be prevented. This, of course, is the key long-range goal of research supported by the NHLBI in this area.

Do warning symptoms precede sudden cardiac death?

There may be no warning symptoms at all, or the victim may complain of sudden severe pain or tightness of the chest or of great difficulty in breathing. The first sign may be the victim's sudden collapse or some other evidence of extreme physiological agitation or stress.

If effective drugs are available for treating cardiac arrhythmias, why aren't they being widely used to prevent sudden death?

Unfortunately, all available and effective antiarrhythmic agents have side effects that make their widespread use inadvisable.

What research is being done on drugs for sudden death?

New, more specific, more effective, and less toxic antiarrhythmic drugs are urgently needed. Once we have them, we must then learn how to administer them to patients selectively on an individual basis, depending on the aspects of the patient's arrhythmia that could lead to ventricular fibrillation.

Is there reason for hope that this can be accomplished?

Some techniques are available to identify high-risk patients, and there are other techniques, which require further development, to define their types of prefibrillation arrhythmias. And a number of promising experimental antiarrhythmic drugs have been developed. Given continued support of these research programs, it should become possible to reduce what is now an unacceptable number of cardiac deaths.

RHEUMATIC FEVER AND VALVULAR HEART DISEASE

RHEUMATIC fever has long been recognized as a cause of rheumatic heart disease, an inflammatory process that involves the heart and its covering membranes. However, the exact mechanisms through which rheumatic fever damages the heart are poorly understood. This disease was extremely common as recently as 30 years ago. Researchers have proved that the process is initiated by a streptococcal infection, usually in the throat. This infection is caused by a type of streptococcus which produces a toxin that, in turn, causes a reaction within the body, producing damage to the heart valves, muscle, and membranes. Millions of persons experienced rheumatic fever and its aftermath, rheumatic heart disease, prior to the development of modern antibiotics and chemotherapy.

Is rheumatic fever still a common and serious problem?

The advent first of sulfonamide and most particularly of penicillin therapy provided an effective and readily available means of treating streptococcal infections and thus preventing rheumatic fever. During the past 30 years the prevalence of rheumatic fever has been reduced strikingly. However, undetected and untreated streptococcal infections and rheumatic fever still occur in thousands of children and in some adults each year, and they still result in serious damage to the heart and heart valves.

What kind of heart damage occurs, and what can be done about this?

One of the most serious consequences of rheumatic heart disease is damage to the heart valves, damage that interferes with their normal function of controlling the flow of blood within the cardiovascular system. The development of open-heart surgery has provided a ready means of correcting most of the serious consequences of valvular heart disease.

In the past, diseases affecting the heart valves commonly resulted in congestive heart failure, disturbance of heart rhythm, and development of intracardiac clots that would often break off and produce occlusion of blood vessels in distant parts of the body. Today we can correct the most serious consequences of valvular heart disease through open-heart surgery and artificial heart valves that permit repair and replacement of diseased tissues, restoring many persons to effective health. However, we have not yet learned how to diagnose streptococcal infection in all children, how to treat all susceptible children long enough to prevent valve deformities, or how to prevent the development of valve deformities in patients who have had an attack of rheumatic fever so mild that it was never recognized as such and never came to medical attention.

What major problems remain with respect to rheumatic fever?

The principal problem today is to assure early detection and prompt treatment of streptococcal infections in order to prevent rheumatic heart disease. Throat infections are common, and many streptococcal infections remain undetected and untreated, so it is not possible to prevent all cases of rheumatic fever. In fact, more than half of the patients with valvular heart disease have no record of a recognized attack of acute rheumatic fever.

Streptococcal infections and rheumatic fever occur most commonly in certain population areas, including Indian reservations, inner cities, and certain

Figure 9. *Congressman Claude D. Pepper (D., Fla.) played a key role in the passage of the legislation that established the National Heart Institute in 1948. Biomedical research that has thereby been fostered has led to the development of lifesaving heart valves and made heart surgery possible. Now, many years later, Mr. Pepper has himself benefited from heart surgery in which damaged coronary blood vessels were reconstructed and a heart valve was replaced. The insert shows a heart valve like the one he uses.*

military reservations, where young people and other highly susceptible persons are exposed to epidemic outbreaks. Early recognition of streptococcal infections permits preventive measures, and prompt treatment usually prevents or lessens heart damage. To date, we can control and prevent the disease in many patients, but not all. Therefore, it is important to continue expanding our knowledge of rheumatic fever to develop the means of cure and prevention.

Over the last 30 years we have come closer to being able to prevent recurrences of acute rheumatic fever and to prevent the development of rheumatic heart disease when the initial attack has eluded preventive measures.

CARDIOMYOPATHIES AND INFECTIONS OF THE HEART

CARDIOMYOPATHIES are disorders of the heart muscle that result from a variety of causes, many of which are unknown or incompletely understood. It has been recognized for many years that bacteria, viruses, and a variety of other microorganisms may invade the muscle, valves, and other structures of the heart, causing infection and inflammation. In more recent years, it has become apparent that other disease problems may be associated with cardiomyopathy; for example, a link between diabetes and myocarditis has been found, although it is not fully understood. The heart may also become involved in

systemic or isolated reactions to toxic substances that result in myocarditis; alcoholic myocarditis also is common and is a serious toxic myopathy.

Heart infections and cardiomyopathies pose a frequent and serious problem in clinical medicine. Infections of the heart can now be managed. Antibiotics have rapidly and profoundly changed the heretofore major problem of curing bacterial infections of the heart valves (bacterial endocarditis). Prior to the development of antibiotics, bacterial endocarditis was almost uniformly fatal. Today most bacterial infections of the heart valves can be cured.

However, cardiomyopathies are more difficult to cure. The medical profession has now become more aware of the existence of *nonbacterial* infections, and of other problems of unknown cause, that result in malfunction of the heart from enlargement (hypertrophy), dilation, and failure. Taken together and treated as a single entity, these diverse disorders constitute a common form of disability and death.

Even though the causes of cardiomyopathies are not completely understood, have there been advances in detecting them?

Several extremely important advances have been made. It is now possible to demonstrate by noninvasive means, through a sonarlike technique known as echocardiography, the presence of thickening of the ventricular muscle septum. In some cases this causes outflow blockage of the left ventricle (the main pump of the heart). Dilation and thinning of the muscular wall of the heart or prolapse (slipping out of place) of a major valve can also be demonstrated by echocardiography. Radiographic diagnosis of defects in the structure and function of the heart muscle has also been strikingly improved with the development of new equipment and technologies (see figure 10).

Is there an effective approach to managing cardiomyopathies?

When cardiomyopathy results from toxic exposure such as alcohol, withdrawal from this exposure often results in resolution of the problem. Similarly, when cardiomyopathy results from a viral process, the problem is often self-limiting. If cardiomyopathy is hereditary in nature, it may be progressive and fatal. There remains a large group of cardiomyopathies of unknown cause that are usually progressive. In this group we have essentially no effective therapeutic approach.

What is the outlook for research in cardiomyopathies and infections and inflammations of the heart?

A number of technological advances, and the development of improved laboratory support systems, such as in virology and immunology, now make research in this complex field practical and opportune. Echocardiography and other approaches to cardiac imaging permit a better description of the anatomy of the heart. Cardiac catheterization techniques have advanced to a point where a catheter biopsy of the muscle or the inner lining of the heart can be accomplished without significant risk. Immunologic and virologic study techniques now permit detailed studies of small portions of the heart to help determine the nature and possibly the causes of abnormalities. An appropriate and opportune time has arrived to make a significant investment in this area of research.

DIABETES

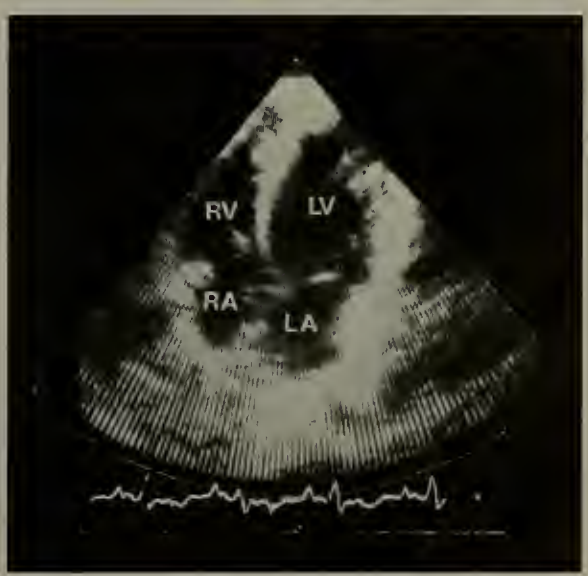
OUR knowledge of diabetes was very primitive until a short time ago. We now recognize diabetes as a complex disease that not only affects a person's ability to metabolize sugar, but also directly or indirectly involves all other body systems, especially the cardiovascular system. Diabetes is characterized by changes in blood vessels, particularly accelerated atherosclerosis, and by accelerated degenerative changes in the nervous system, including the brain. Diabetes is one of the four major contributors to atherosclerosis. Many of its worst complications—those affecting the eyes, kidneys, heart, brain, and legs—involve the blood vessels. More than 75 percent of diabetics die of cardiovascular disease. There are two types of diabetes—juvenile and maturity-onset—usually distinguished by the age at which symptoms appear. About 10 percent of diabetics have juvenile diabetes, which usually begins before age 25. In this form adverse effects occur faster and earlier.

Diabetes is one of those ancient diseases against which little progress was made prior to this century. As early as 1650, diet had been prescribed for diabetes, and nearly 200 years later exercise was added.

Figure 10. *Great advances have been made over the last 30 years in imaging (looking at) the heart. The top picture shows a chest X-ray taken in the 1940's. All that can be told from such pictures is the overall size of the heart and the shape of the silhouette. The internal cardiac structures are not visible, nor is it possible to determine whether the shadow is created by an enlarged heart or whether there might be fluid in the sac surrounding the heart.*

The lower left picture shows a more recent and refined technique, called an angiogram. Not only is the shape of the heart clearly seen, but the coronary blood vessels are shown as well. This is an invasive procedure which requires placing a small plastic tube (catheter) in the arteries of the heart. The place marked by an arrow shows an obstruction of one of the vessels, a sure sign of disease.

On the lower right is an even newer, noninvasive and safe technique, called echocardiography. A cross-sectional view is given, with the four chambers of the heart shown upside down (RA and LA = right and left atria, RV and LV = right and left ventricles). This is a single frame taken from a movie which can section through many levels of the heart in sequence. The size and shape of each chamber, and thus the exact position of any diseased area, can be determined. The trace at the bottom of this picture is an electrocardiogram, which depicts the electrical activity produced by the heart as it beats.



Neither therapy was very helpful unless the diabetes was mild. As recently as 1920, diagnosis of diabetes was still a sentence of early death—especially in a young person. The diabetic was doomed to a relatively short life marked by devastating complications, and many died within months after diagnosis.

Have there been recent advances against diabetes?

The outlook for diabetics changed radically in 1922, when insulin was discovered. Since then, insulin injections (and oral hypoglycemic drugs, which became available in 1955) have been averting early death for millions of diabetics. There is still no cure for diabetes, but it can be controlled by an individually regulated combination of insulin or oral medication, diet, exercise, and sometimes weight reduction.

If we can control diabetes, why is it still a major problem?

Control only slows the disease; it does not stop its progress or its complications. We need more effective control, and a means of cure and prevention.

Figure 11. *Noninvasive tests are used to diagnose heart disease. The physician, in the center, is imaging (viewing) the patient's heart using echocardiography. An instrument which emits high frequency sound waves is held over the patient's heart. The echoes bounce back at different frequencies and thereby reveal the exact location of any diseased heart tissue. The image of the heart is viewed on a screen.*

In the background is another patient, who is exercising on a treadmill while his heart function is being tested. This type of test can reveal some problems that are not evident when the patient is tested at rest lying down. Research to develop and refine diagnostic tests for heart disease has been particularly fruitful during the last decade.

Despite drug treatment, dietary control, and adequate exercise, at any age a diabetic's remaining life expectancy is about two-thirds that of a nondiabetic. Without treatment it is far less. In addition, all of these millions of diabetics, treated or not, still risk severe and often fatal complications.

What are the complications of diabetes?

Just as diabetes can affect all of the body's systems, so can its complications. *Diabetes plays a major role in heart attack, stroke, kidney disease, gangrene of the feet and legs, nerve damage, and blindness. The diabetic patient is twice as prone to heart disease as the general population, and five times as prone to gangrene (which frequently results in amputation). Diabetes is also the leading cause of new cases of blindness.* Of the many deaths attributed to diabetes, 75 percent are due to some form of cardiovascular disease. Diabetes is the fifth ranking cause of death in the United States.

Economists estimate that diabetes costs the nation more than $5 billion a year in health care, disability payments, and lost wages. This does not include the additional high cost of cardiovascular and other complications, to which diabetes is one of the four major contributing factors.

How is cardiovascular disease related to diabetes?

We are not yet sure. However, recent research has discovered pathological changes in the blood vessels and blood components of diabetics. These changes may explain why most people with diabetes die from cardiovascular diseases.

Two kinds of disorders in the blood vessels of diabetic patients lead to different kinds of complications. One kind is found in the smallest blood vessels, the capillaries, and is therefore called *micro*angiopathy; this leads in particular to diseases of the eye and kidney. The other kind occurs in the larger blood vessels, especially the arteries, and is called *macro*angiopathy; this leads to heart attack, stroke, and gangrene of the extremities. These changes may be due to alterations of platelet function and of the hemoglobin molecule that have been found in diabetic patients. Such platelet and hemoglobin changes may contribute to the development of macroangiopathy and microangiopathy.

We still do not know the cause of any of these changes. Research to find better treatment and a means of cure and prevention is imperative.

How close are we to a better understanding of these problems?

We do not know. Basic and clinical research are underway on many aspects of diabetes. Research supported by the NHLBI is focused especially on those aspects of the cause, pathology, and complications of diabetes that act through and affect the cardiovascular system.

The Institute currently supports a variety of research studies directly related to diabetic macroangiopathy and to the diabetic state as it affects cardiac disease. For example, important risk factor and epidemiologic data on heart disease and diabetes have emerged from four long-term community heart studies supported by the NHLBI. These are the Framingham, Tecumseh, Chicago, and Honolulu heart studies, each of which covers a span of approximately 30 years. Moreover, many basic and applied studies and clinical trials concerning heart and vascular disease, while not directly related to diabetes, are considered to have potentially important impact on the prevention or mitigation of cardiovascular complications in diabetics.

Most important, we know today that diabetes, cardiovascular diseases, and metabolic, endocrine, and other bodily processes are so inextricably intertwined that basic and clinical research advances in any of these areas must inevitably affect, and be affected by, advances in the others. In addition, since diabetes affects many body systems besides the cardiovascular system, diabetes research is also being supported by other institutes of the NIH. The combined impact of all these studies will no doubt speed progress toward better control of diabetes, and perhaps even toward cure and prevention.

Figure 12. *This 4-year-old child has diabetes. In many respects she leads a normal active life, playing, swinging, and climbing like any other youngster. Because she is so young, her parents currently administer the lifesaving injections of insulin. However, she is already beginning to learn injection techniques by practicing with a syringe on her doll, so that eventually, when she is about 7 or 8, she will be able to inject herself.*

LUNG DISEASES

WITH respect to accomplishments in lung research and the management of pulmonary diseases, two examples are discussed to illustrate the different problems and stages of development that exist in our knowledge of such disorders.

Chronic obstructive lung disease is now recognized with much greater frequency. Its association with smoking has been identified, but much remains to be discovered concerning its cause. *Adult respiratory distress syndrome* has been more recently identified with a variety of acute traumatic and other type disorders. We still know little concerning the cause, management, and prevention of this problem, which is also being recognized with increasing frequency.

Some recent advances in management and diagnosis of pulmonary diseases, and in knowledge of the structure and function of the lung, are also reviewed briefly.

CHRONIC OBSTRUCTIVE LUNG DISEASE

CHRONIC obstructive lung disease is a disease entity that includes the basic clinical features of both emphysema and chronic bronchitis.

A typical patient with chronic obstructive lung disease is a middle-aged man who smokes cigarettes and has a chronic and recurrent cough. At first he coughs only in the morning, but later he coughs intermittently throughout the day. As time goes by, in addition to the cough, he is bothered by shortness of breath. This often starts simply as a vague feeling of discomfort during exertion, such as when he climbs a flight of stairs or runs to catch up with a colleague. Eventually, the cough and breathlessness worsen. The breathlessness is present even when the patient walks slowly on level ground, and it progresses inexorably until he is short of breath even when sitting quietly in a chair.

Near the end of his life, the breathlessness is often so severe that the patient cannot sleep. At some point in this last phase of the disease he will probably have a pulmonary infection. If so, he may rapidly become critically ill, with periods of respiratory failure.

This dramatic disease has a long and fascinating history. Its recorded history may have begun in the 2nd century A.D. with a description of a breathless patient by Arateus. Arateus said the man constantly hungered for air and was suffering from "the asthma," but the symptoms described could just as well have been those of chronic obstructive lung disease.

Through most of the centuries since Arateus, chronic obstructive lung disease received little attention. As recently as 30 years ago, it was often not recognized and was considered relatively unimportant. *Since about 1950, its status has changed spectacularly—having evolved from an uncommon entity to number 7 among the nation's top 10 killers. It also accounts for the third highest cost in disability payments, exceeded only by mental illness and heart disease (see figure 13).* Half of the patients disabled are wage-earning husbands and fathers under age 60; thus, in addition to the misery imposed on the patient, the disease affects countless other lives.

Has there been any progress against chronic obstructive lung disease?

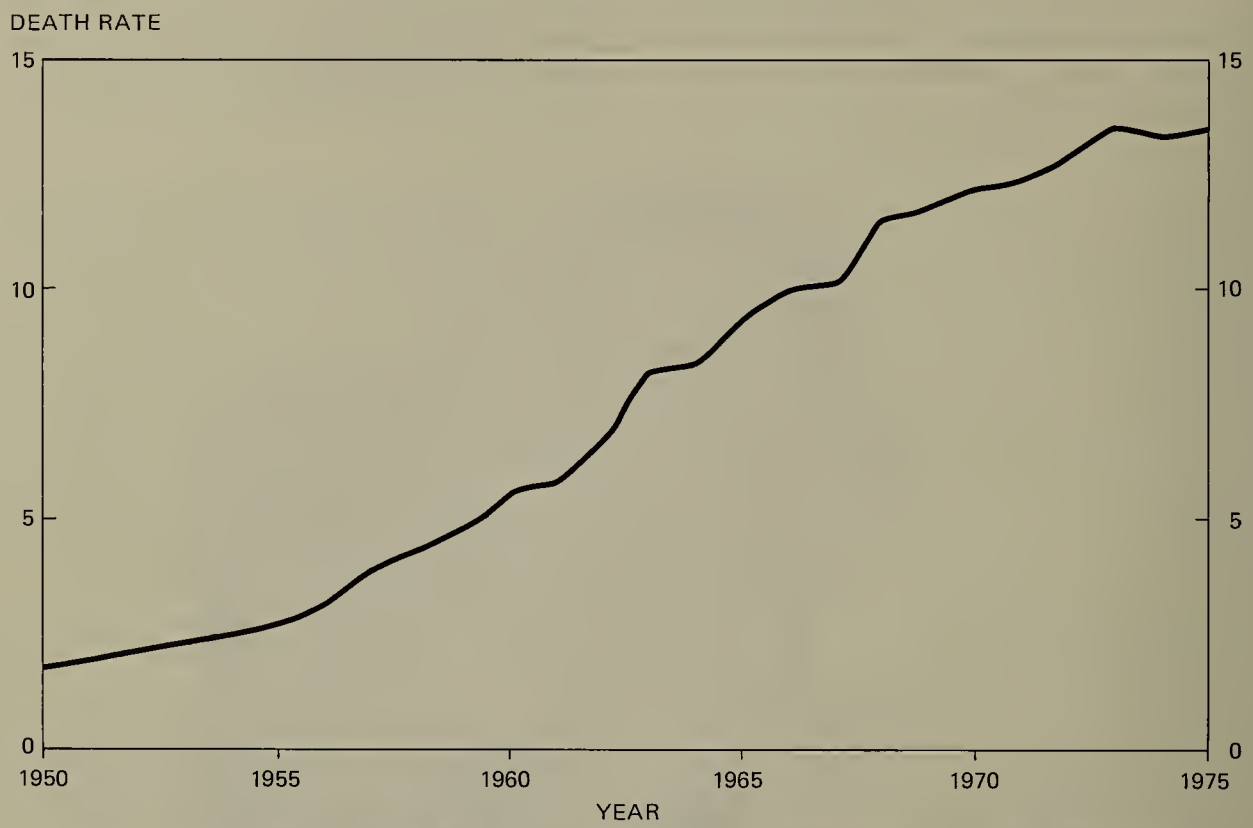
Thirty years ago we would have thought it impossible to reverse the physiological changes that occur in obstructive lung disease and in its characteristic episodes of severe respiratory failure. Today we know that with critical care medicine we can improve breathing in some people, and we can restore these people to a fairly comfortable life. This is because investigators have perfected mechanical ventilators that help the patient breathe through periods of severe respiratory failure.

Do we know the cause of obstructive lung disease?

No, but we do know a major contributing factor, perhaps the major factor. No other clinical research development during the 30-year history of the NHLBI—the period in which this disease has been coming steadily to the forefront—has been more important than the discovery and confirmation of its link to cigarette smoking. We now know that in most patients the disease develops during long exposure to cigarettes. With few exceptions a patient who has chronic obstructive lung disease is a cigarette smoker or has been one over a period of some years.

How does obstructive lung disease damage the pulmonary system?

Figure 13. *Death Rate for Chronic Obstructive Lung Disease, U.S., 1950-1975.*



Chronic obstructive lung disease includes emphysema and chronic bronchitis. Death rate reported per 100,000 persons, age-adjusted to 1940 U.S. population.

Source: National Heart, Lung, and Blood Institute from data from the National Center for Health Statistics.

In healthy individuals, the lungs and bronchial tubes have an efficient self-cleansing system. Tiny glands in the walls of the airways secrete mucus that absorbs inhaled dust and other foreign particles, including bacteria. The cilia (small hairlike structures on the inner walls of the major airways) sweep the mucus and its load of entrapped foreign matter upward and outward for removal as sputum. *In individuals with advanced chronic obstructive lung disease, this self-cleansing system is no longer able to protect the lungs effectively.* The mucus and cilia that normally move inhaled particles and bacteria through the airways do not work as well as they should. In addition, deterioration occurs in the thin walls of the alveoli, the tiny air sacs where the blood exchanges carbon dioxide for fresh oxygen. The breakdown of the alveoli constitutes irreversible loss of breathing capacity.

How has the outlook for patients with obstructive lung disease improved?

Major advances have been made in handling episodes of acute respiratory failure, but the death rate remains very high. The physician can now help the patient with oxygen, antibiotics, and an assortment of ventilatory and other devices. *But the possibility of a person with this disease recovering from an episode of complete respiratory failure is probably no better than two chances out of three.*

As recently as 1950 the odds were much worse. *One of the direct benefits of investigation in the past*

30 years has been to teach us how to handle acute respiratory failure.

Are there any steps we can take to prevent chronic obstructive lung disease?

Yes, we can convince people to stop smoking—or even better, never to start. Our progress with this problem is much too slow. If any single problem engages our attention, it should be the discouragement of smoking.

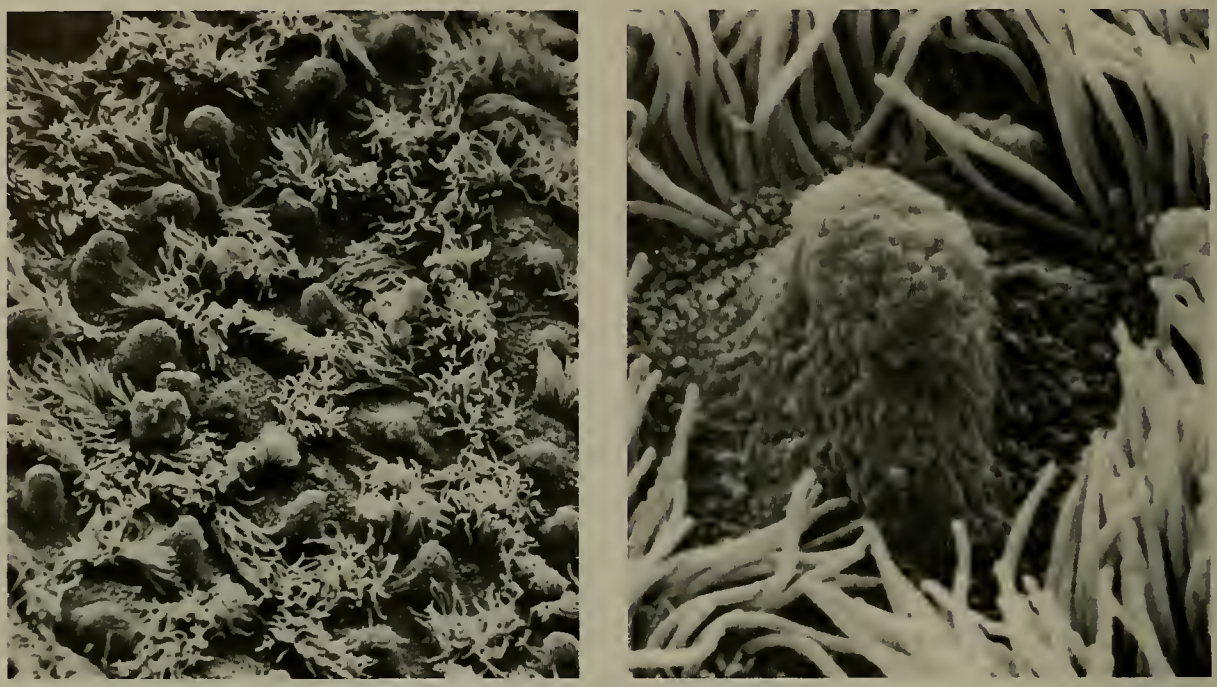
Can we honestly promise any benefits worth the struggle the smoker may have to go through to stop?

Most people with pulmonary damage caused by smoking have had the habit for many years. To break this habit requires considerable behavioral change. Our antismoking campaign should be much more effective if we can promise the smoker a substantial benefit of improved health. *And the fact is that we can.*

Physicians can assure smokers that, if they stop smoking, the levels of oxygen and carbon dioxide in their blood will almost always improve and may become normal—no matter how long they have been smoking. Moreover, the abnormal flow of air in their airways will improve. However, once the disease has advanced to the point of chronic cough and breathlessness, stopping smoking will not return the lungs to normal. It will not restore the structure of broken-down alveoli. Structural losses will remain, and the scarring will not improve even if the patient never smokes again. *But whatever the state of the lungs when a person stops smoking, they do function better,* often markedly better, and further deterioration, if there has been any, will be slowed.

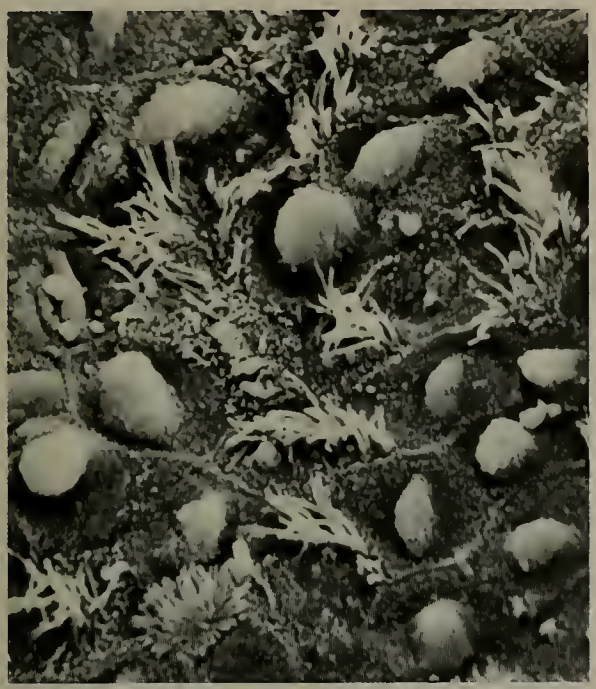
Once the lung structure is damaged, the damage cannot be repaired; but other effects *can* be repaired—ciliary function can be restored, and whatever lung structure remains intact then works better. Does this amount to a structural gain?

Figure 14. *Teenagers discuss the health hazards involved in smoking. In these discussions they learn about the pressures that may induce them to start and are advised how to resist. This is part of the Smoking in Schools Project funded by the NHLBI.*



A B

Figure 15. *These are electron micrographs of cilia in the lung. The cilia are damaged when lung bronchioles are exposed for varying periods of time to nitrogen dioxide (NO_2). This substance is a component of photochemical smog and is also found in cigarette smoke once the NO_2 molecules resulting from the burning of protein in the cigarette have had an opportunity to react with oxygen in the air. It has been calculated that a puff of cigarette smoke contains at least 25 parts per million of NO_2 by the time it reaches the lower end of the respiratory tract, which is the area depicted in these pictures. On the top left are two pictures (A, B) of a normal terminal bronchiole of a rat at two levels of magnification (x 2,800, and x 14,600). Normal bronchioles have many active cilia, hairlike structures which are evenly distributed and interposed with nonciliated epithelial cells rising above the bronchiolar bed. The loss of cilia (C) is apparent after 24 hours of exposure to 15 parts per million of NO_2 (x 4,300). After continuous exposure to this level of NO_2 for 48 hours (D), the surface of the bronchiole becomes flattened and the cilia are almost completely lost (x 4,300). The extensive loss of cilia prevents their normal clearing function in the distal airways.*



C

D

Yes. But we can be more specific about what happens when a person with this disease stops smoking. His cilia work better, he eliminates his mucus and foreign matter more efficiently, and his airways offer less resistance to breathing.

Another change also takes place—an extremely important change that people have heard too little about. This has to do with the hemoglobin in the red blood cells. In people who smoke heavily, as much as 10 percent of the hemoglobin is monopolized by carbon monoxide and is therefore no longer available to carry oxygen. In people who do not smoke, or who stop smoking, *all* of the hemoglobin is available to transport oxygen to every part of the body.

Obstructive lung disease is a complex process. For the most part, it is in some way initiated or activated by exposure of the lung and its supporting structures to toxic substances such as tobacco smoke. We know the link to tobacco but not the specific cause or the reason for the toxic response. The mechanism of this malfunction needs to be much better defined. Whatever other factors may be involved, avoidance of tobacco will greatly improve public health. However, to define the cause and cure of obstructive lung disease, and ultimately to discover a means of prevention, will require concerted basic and clinical investigations.

ADULT RESPIRATORY DISTRESS SYNDROME

LIKE infant respiratory distress syndrome, adult respiratory distress syndrome is characterized by shortness of breath, due to an inability to absorb enough oxygen. Unlike the condition in infancy, however, adult respiratory distress syndrome occurs in a variety of situations. We see it, for example, during or after trauma, especially severe trauma such as people sustain in automobile accidents. We also see it in adults after surgery and during severe lung infections. In short, adult respiratory distress syndrome may occur in almost any extremely stressful situation accompanied by severe damage to the body.

A person with adult respiratory distress syndrome almost always complains of breathlessness. He or she may be so short of oxygen that the skin will be

cyanotic, or blue. In addition, oxygen cannot be satisfactorily absorbed and the oxygen levels of the blood are therefore usually abnormal. If the abnormalities are great, the organs and tissues become "distressed" and malfunction. When we examine the patient's lungs, we find them to be inelastic and stiff. X-rays routinely show that the disease is diffusely scattered throughout both lungs.

Death statistics on adult respiratory distress syndrome are appalling. Until just a few years ago, the disease was invariably fatal. Even today, about one out of three patients dies despite modern treatment techniques and the very best possible management. This condition of the lungs is far from solved.

What causes adult respiratory distress syndrome?

We know that the problem is associated with body stress and injury, but the mechanisms of the disease are unclear. All the physician can do for a patient who is critically ill with the respiratory distress syndrome is to try to support his or her respiratory function.

Is this a condition where the lungs have been diseased for a long time, as in chronic obstructive lung disease?

No, the patient is apparently normal before sustaining the body injury. People who develop adult respiratory distress syndrome usually have *normal* lungs before they are exposed to the stress of severe trauma such as an automobile accident, major surgery, or an acute infection. Indeed, the lung complication grows out of the inciting event, and it is this complication that often leads to death.

Patients with this syndrome have to be managed in a critical care unit. Here, physicians use the new tools and techniques that clinical investigators have developed over the past 30 years. Oxygen is given under carefully controlled and monitored circumstances. Respiratory machines are used to ventilate the patient who is too weak to expand his stiffened lungs. A small catheter may be "floated" into one of the blood vessels of the lungs in order to measure the pulmonary blood pressure and the rate of blood flow in the lungs. These measurements are essential in order to properly adjust the ventilator that is breathing for the patient, and to decide whether to take other steps that might be beneficial, such as using drugs to sustain the blood pressure and using nutritional and mineral replacement fluids.

Treatment is important, but what causes the disease?

We do not have the answers yet. A number of theories as to cause have been advanced. One theory is that a great number of white blood cells get trapped in the lung, disintegrate, and discharge enzymes. These are enzymes that normally protect us against infection; here, however, the white blood cells are in such great numbers that the enzymes actually attack the lung.

Since we do not know the cause, is this the goal of current research?

This is one of the goals. We cannot predict the directions from which new advances may come. However, the most recent advance is an effective management tool. This is the use of positive end-expiratory

Figure 16. *The trauma of a car accident such as this one, in which children and adults were injured, can sometimes result in the onset of adult respiratory distress syndrome, a serious lung complication that can lead to death.*

pressure, a simple maneuver in which the patient breathes against a constant pressure. As a consequence, areas of the lung that have collapsed open up, expand, permit air exchange, and help oxygenate the blood. Even if the patient survives the acute episode of respiratory distress, there is still danger. Some patients recover normal lung function; but some begin to accumulate scar tissue, and this seriously interferes with the lung's ability to exchange oxygen and carbon dioxide.

We have made progress, albeit limited, in recognizing and understanding this problem. We can prevent death in a significant number of people who would formerly have died—but a major breakthrough depends on further research.

OTHER ADVANCES IN PULMONARY DISEASES

OTHER advances have been made in management and diagnosis of lung diseases and improved understanding of the structure and function of the lung.

What is critical care medicine?

The growing importance of chronic obstructive lung disease, with its periods of exacerbation and improvement, gave rise to a new concept—the critical care of patients whose lungs have failed.

Prior to the use of mechanical respirators to sustain patients with poliomyelitis, treating patients with respiratory failure was viewed as a futile exercise. But the collaboration of engineers and physicists with physicians and physiologists produced new types of respirators that could temporarily take over a patient's breathing, and these machines led to the concept of critical care.

These respirators were also used to prolong the lives of patients with obstructive lung disease. The machines enabled physicians to tide patients over episodes when the lungs had temporarily failed, along with the rest of the body's respiratory apparatus. The same machines were then used successfully in people with other acute illnesses or injuries—severe pneumonias, pulmonary burns, overdoses of drugs, chest wounds or trauma, and respiratory distress syndrome in both adults and infants.

Have there been many advances in diagnostic techniques?

Yes, a large number. Just as engineers and physicists helped to develop mechanical respirators, they also joined again with physicians and physiologists to perfect new diagnostic techniques. For example, they produced small electrodes that could sample the levels of oxygen and carbon dioxide in the blood. Thus, it became possible to assess the way the lungs were aerating the blood, and to monitor the effects of therapy accurately and continually. Scientists also used radioactive isotopes to measure pulmonary function. By combining isotopes that could be inhaled with others that could be injected, physicians could estimate the flow of air and blood in various parts of the lung. Later, engineers produced small glass fibers with diameters no larger than those of fine threads, which could be bundled together in a long, flexible fiberoptic cylinder and used to look deep within the lungs. A small knife set to one side of the bundle of fibers could snip off a piece of lung tissue, thus enabling pathologists to make diagnoses—and physicians to prescribe appropriate therapy—without having to operate on the chest.

Obviously, the two examples of lung disease discussed here—chronic obstructive lung disease and adult respiratory distress syndrome—represent only a fraction of the whole area of lung disorders. Speaking more broadly, what major advances have been made in recent years in our understanding of lung function?

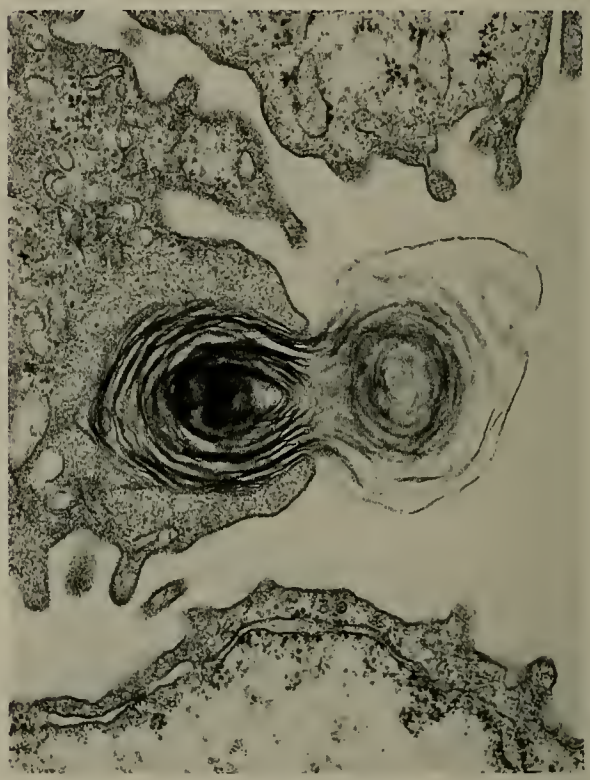
The following are a few of the many advances in the science of respiratory physiology:

- The lining of the lung has been shown to be a thin layer of liquid that behaves like a detergent. Named surfactant, the liquid lines the alveoli, the small air sacs where gas exchange occurs, and helps to stabilize them.
- The responses of the lung's blood vessels to different stimuli have been systematically identified and studied. This led to the discovery that lack of oxygen constricts these blood vessels, even though it dilates vessels in other parts of the body.
- The effects of inhaled irritants, especially the byproducts of industry, have been assessed.

- The cells of the lungs have been subjected to the same scrutiny as the cells in other parts of the body, with the result that the functions of the different cells have become well-known. Macrophages, for example, have been found to serve as scavengers in the lung, just as they do in other parts of the body, thereby protecting the lung from foreign material carried to it through inhaled air. Other cells produce the detergent-like surfactant that lines the alveoli (see figure 17). Still others secrete mucus, which becomes a veritable fluid blanket lining the airways, so that the cilia can propel the blanket upward, thus delivering dust and dirt to the nose for expulsion.
- The lung has been shown to take part in immunologic reactions, some beneficial and some causing disease.
- The lung has been found to contain enzymes, especially one that converts a substance called angiotensin to an active form. Once activated, angiotensin helps control the level of blood pressure.
- Pediatricians have found they can predict—even before a baby is born—whether the child will develop neonatal respiratory distress syndrome. The technique entails sampling of amniotic fluid from the mother. Thus forewarned, physicians are now able to save the lives of the majority of these babies.

Expanding knowledge of physiology has changed the nature of research on the lung. Thirty years ago, investigators looked mainly at gross functions—for example, the performance of the chest as a bellows to move air. Today, research effort is directed at the functions of individual cells and the products of these functions, such as surfactant, connective tissue, enzymes, and mucus. The hope is eventually to understand these basic functions, and perhaps to discover how an abnormality in one or more of them triggers the development of disease.

Figure 17. *This electron micrograph shows a Type II lung cell in the process of secreting surface-active material into the air space. Once secreted, the material will form a thin film covering the lung cells, which helps maintain efficient and stable patterns of breathing.*



BLOOD DISEASES AND BLOOD RESOURCES

REMARKABLE progress has been made during the past 30 years in the detection, treatment, and prevention of blood diseases, and in the use of blood to save life and to perform what used to be considered "impossible" surgery.

Blood diseases have been recognized for centuries because of the relatively easy access to blood for examination. Human blood was one of the first substances to be examined under the microscope over three centuries ago. Both red and white blood cells were recognized then, and the much smaller platelets in the circulating blood were identified microscopically about 200 years later. In the circulation these formed elements—red cells, white cells, and platelets—are suspended in the liquid blood plasma.

The best known of the *bleeding disorders*, hemophilia, can now be treated, and severe bleeding prevented, by intravenous administration of a blood component that is present in normal blood but is missing from the blood of hemophilia patients. The missing component is prepared from normal blood plasma.

Increasing knowledge of the mechanisms of normal blood clotting and the central role of the *platelets* in clotting has important implications in diseases marked by *thrombosis*, the abnormal occurrence of clots that impede or block blood flow.

Great progress has been made in the control and treatment of *anemias*. Almost all nutritional anemias can now be effectively treated. In addition, increased knowledge of hereditary anemias such as sickle cell disease and thalassemia offers promise of future control of these disorders.

Our greatly improved knowledge of blood and *blood resources*, including blood types, blood preservation, and storage, has made possible safe blood transfusion, without which many major surgical procedures, including open-heart surgery, would be impossible.

BLEEDING DISORDERS

BLEEDING disorders are diseases in which the blood does not clot properly. Hemophilia is the most widely known bleeding disorder. The victim may literally bleed to death from a relatively minor injury simply because the blood will not form a clot.

Is the process of blood clotting well understood?

The phenomenon of blood coagulation is familiar to everyone, but learning how the process works has taken a very long time. Prompt cessation of bleeding following a cut serves as a reminder that the body has a process that will usually stop the loss of blood.

Two main classes of blood components are involved in the phenomenon of blood clotting: proteins in the blood plasma, and tiny formed elements known as platelets. Much of our knowledge of the substances involved in blood clotting has accumulated in the last 30 years. Better understanding of the functions of some 15 or more different clotting factors in the plasma has resulted from the study of bleeding problems in patients with familial defects. Studies of hemophilia and other coagulation-factor deficiency states have provided a solid but still incomplete fund of knowledge of the normal clotting process.

Has hemophilia as a bleeding problem been conquered? What is the cause of this disorder, and can it be prevented?

Hemophilia has been recognized for centuries. It is suggested in the Talmud that circumcision is not necessary in certain instances where bleeding has occurred in the family. Hemophilia was a much publicized disease of male members of some of the royal families of Europe, to whom it was apparently transmitted through the daughters of Queen Victoria.

We now know that the cause of hemophilia is the lack of a clotting factor that is present in adequate amounts in normal blood. In the 1940's it was demonstrated for the first time that the prolonged clotting time of the blood of individuals with hemophilia could be corrected by the addition of fresh normal plasma. This was the beginning of replacement therapy with fresh plasma. Prior to this time most hemophiliacs died of blood loss or of bleeding into vital organs following relatively minor trauma. However, transfusions with plasma or whole blood were cumbersome. They could not be given in the necessary amounts or with the necessary frequency to prevent such crippling complications of hemophilia as chronic arthritis from frequent bleeding into joints of the arms and legs.

Research of the last 30 years has resulted in a drastic change in the outlook for patients with hemophilia, not only for survival but also for quality of life. The change followed the discovery that normal blood contains an antihemophilic factor. Today, the availability of a preparation of concentrated antihemophilic factor has permitted many hemophiliacs, who can administer the antihemophilic factor to themselves, to lead nearly normal lives with greatly reduced disability and deformity. Use of concentrated antihemophilic factor now makes it possible for hemophiliacs to undergo surgery, including open-heart surgery, when needed (see figure 18).

This does not mean, however, that the problems of hemophilia have been solved. Treatment with antihemophilic factor amounts to replacement therapy and involves the use of a substance derived from human blood. It is not a cure; it is expensive and constitutes a significant drain on the national blood resources. Thus the scientific community is still faced with the challenge of developing a curative form of treatment, which can be achieved only through painstaking biomedical research.

Besides hemophilia, there are a number of other recognized blood coagulation defects. The detection of persons or families with these less common bleeding problems has permitted extensive study of the sequence of events in the coagulation process. Treatment of some of these disorders is now possible through blood component replacement; however, the resolution and prevention of these disorders is still a challenge. Indeed, effective scientific study of the highly complicated process of blood coagulation is probably still in its adolescence, and much of the research in bleeding disorders may ultimately have major implications for thrombosis.

Figure 18. *An oral surgeon and a hematologist examine the mouth of this hemophilic patient to insure that there is no bleeding after recently completed oral surgery. The patient had received preoperative treatment with concentrated antihemophilic factor prior to the recommended surgery. Antihemophilic factor is essential to prevent the bleeding expected from the surgery. Following surgery, such a patient would be treated with additional antihemophilic factor concentrate and/or antifibrinolytic drugs. Such surgery would not have been possible a few years ago because bleeding would have continued unchecked.*

PLATELETS AND THROMBOSIS

PLATELETS are tiny formed elements of the blood (see figure 19) that are made in the bone marrow and released into the blood stream, where they survive for only a week or so. Platelets have been recognized for many years, but the complexity of their structure has been realized only with electron microscopy during the last 20 years. When a blood vessel is injured, platelets collect promptly at the site of injury to form a platelet plug or seal to slow or stop the bleeding (see figure 20). Platelets are also important in the formation of the clot at the site of injury.

How do platelets participate in blood clotting?

Platelets contain or carry on their surface many different substances, some of which result in constriction of the blood vessel. The proteins they carry initiate the clotting process. Many plasma proteins interact sequentially, and finally a clot of insoluble fibrin is laid down at the site of injury. Platelet-borne enzymes also play a role in the subsequent contraction of the clot and in the healing of the injured vessel.

Do platelets play a role in abnormal coagulation problems such as occur in heart attack, stroke, or thrombophlebitis?

Figure 19. *This electron micrograph shows four platelets and a doughnut-shaped structure which is a normal red blood cell. In front of it is one platelet, and three others are seen on the right (magnification x 20,000).*

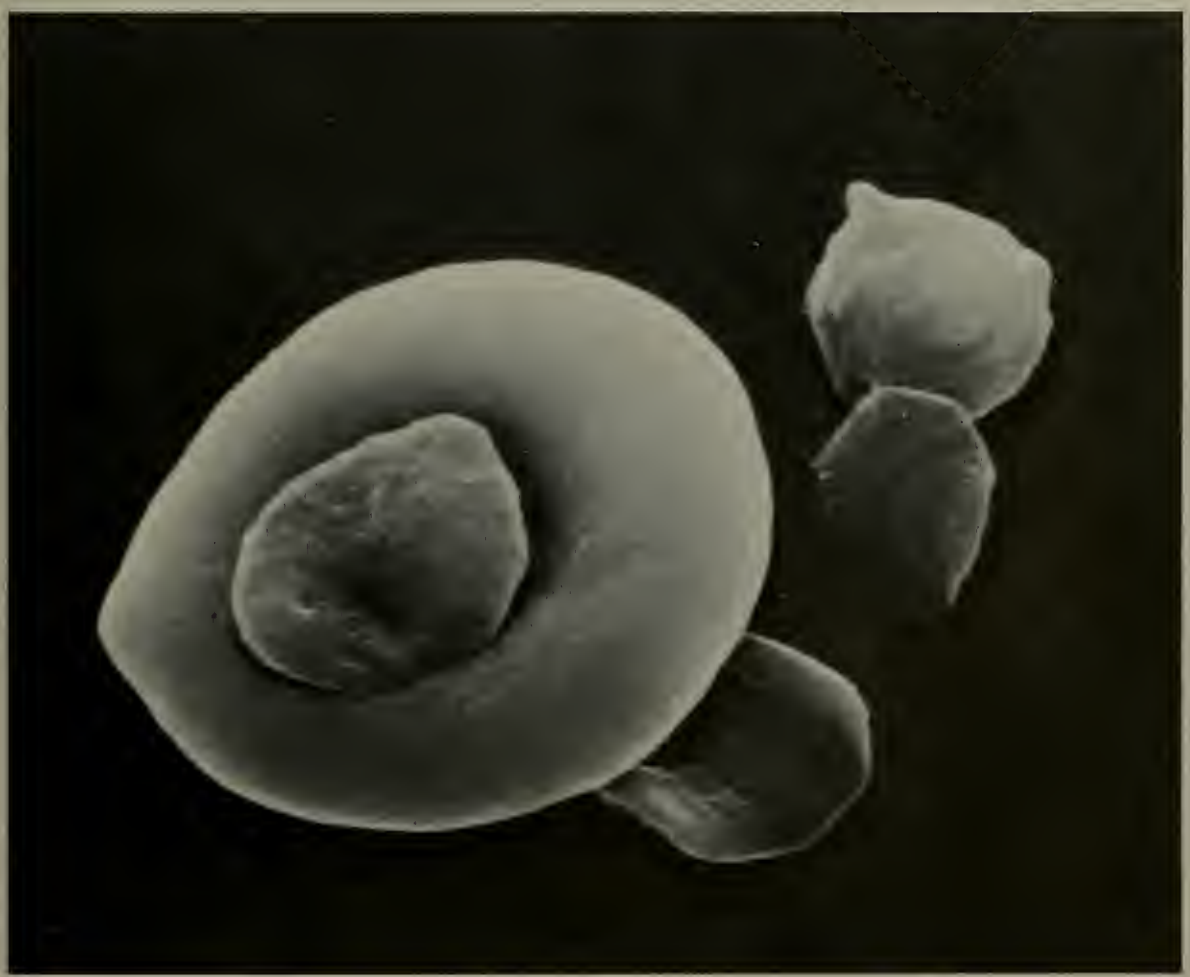
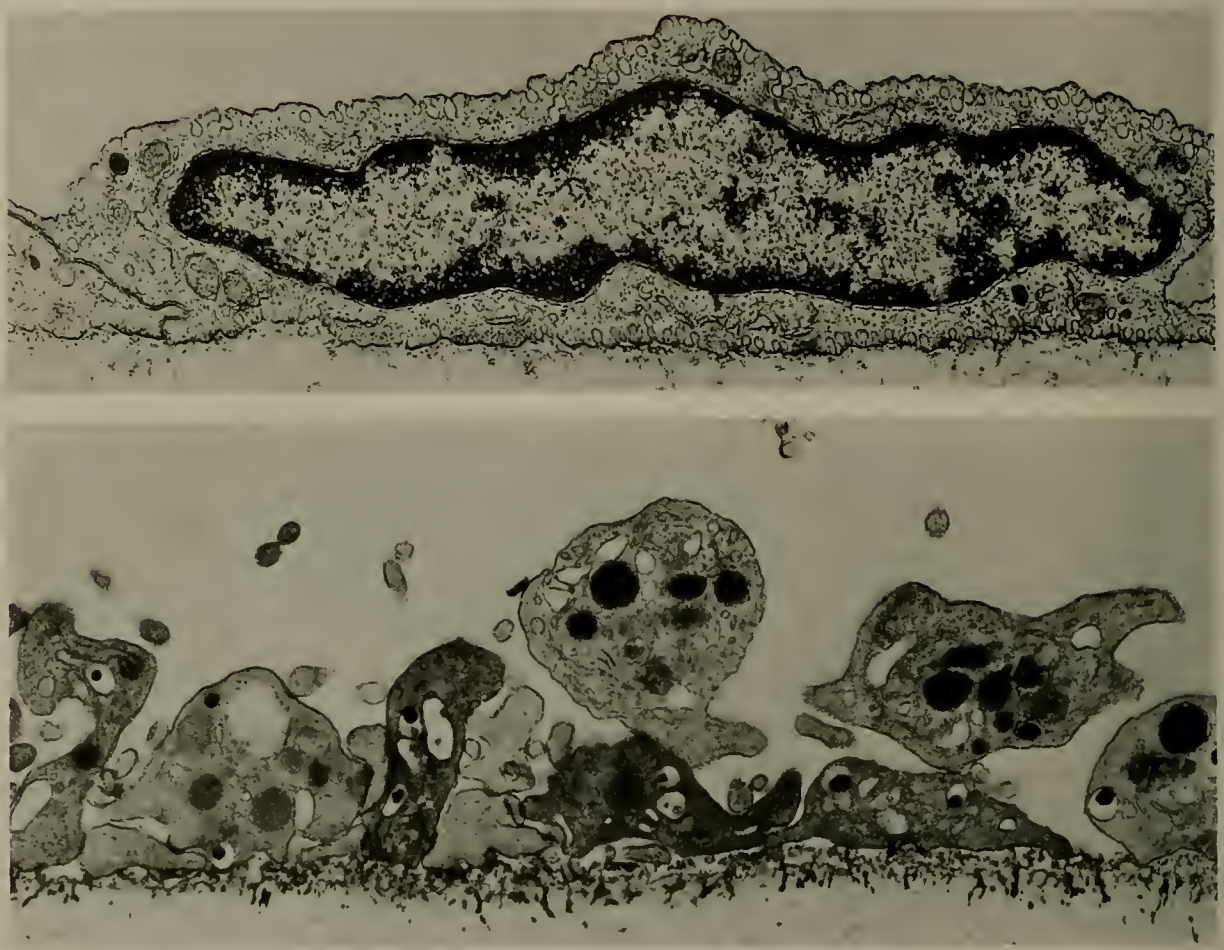


Figure 20. *On the top is a normal arterial blood vessel wall. On the bottom is an injured vessel wall which has been damaged by a balloon catheter. Platelets (small round structures) collect at the site of the injury and are seen here sticking to the blood vessel lining. In each picture, the inner surface of the blood vessel faces toward the top (magnification x 20,000).*



Recently, increasing evidence has suggested that platelets may play a role in the clotting process that may accompany coronary or cerebral thrombosis, as well as in other disorders such as thrombophlebitis. In many disorders a diseased blood vessel becomes the site of platelet aggregation; in other disorders the platelets themselves may be abnormal.

Are there diseases in which it is desirable to diminish the normal process of blood clotting?

A number of problems, such as cerebral ischemic episodes (small, transient strokes), apparently may be initiated by clumping of platelets and subsequent clotting. Approaches to impairing such clotting by use of agents that interfere with platelets—for example, aspirin—are being studied. Traditionally used therapeutic agents, such as warfarin sodium, interfere with the synthesis of some of the plasma proteins involved in coagulation.

Are other areas of research involving platelets and the coagulation process likely to prove fruitful?

Yes, but there are many areas that need to be investigated.

Thrombosis is important in all blood vessel diseases, for example, coronary artery disease, stroke, and the vascular disease of diabetes. Only in the last several years have we begun to recognize that platelet involvement may be important in these diseases. The normal blood vessel lining may itself inhibit the aggregation of platelets, while a damaged vessel will interact with platelets to result in formation of a platelet clump at the site of injury and in the development of atherosclerotic lesions. Thus local vessel-and-platelet interaction may be important in the initiation of atherosclerotic plaques in vessels. These plaques may enlarge by successive injury-and-repair mechanisms in which the platelets not only clump at the site of injury, but also later promote the smooth muscle proliferation of repair. Successive atherosclerotic vessel lesions, with their lipids, scar tissue, and increased smooth muscle, steadily reduce the inner diameter of the affected blood vessel.

ANEMIAS

ANEMIA usually refers to a decrease in circulating red blood cells and their principal constituent, hemoglobin. The red cells and hemoglobin are produced in the bone marrow, and the cells are released into the circulation, where they normally survive for about 4 months.

Anemia may result from (a) deficient production of red cells or hemoglobin, (b) premature destruction of red cells by dissolution (hemolysis), so that their survival is only a few weeks rather than 4 months, or (c) loss of red cells by bleeding, as in extensive injuries or in bleeding from a peptic ulcer or menstruation. In addition, anemia often occurs as a secondary development in disorders that are not primarily blood diseases. In kidney failure or severe arthritis, for example, red cell production may become defective and anemia will develop.

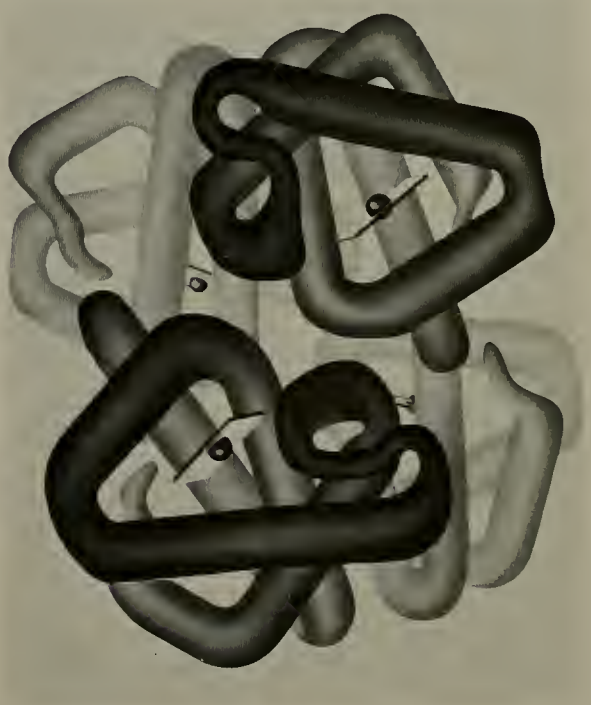
The symptoms of anemia result from reduced availability of oxygen to the body as the hemoglobin level falls. Patients are often pale and complain of weakness, fatigue, and palpitations.

Why is hemoglobin important to the body?

Hemoglobin is an oxygen-carrying protein contained in the red blood cells. Hemoglobin has unique properties that enable it to pick up oxygen as the red cells circulate through the lungs, and to release the oxygen wherever it is needed, for example, in the heart, brain, or muscles. After the hemoglobin gives up oxygen, the red cells return to the lungs to pick up more oxygen. On the way back to the lungs, they carry carbon dioxide picked up from the tissues.

Thus hemoglobin is the carrier of oxygen from the lungs to all the organs, tissues, and cells of the body. This function of hemoglobin began to be appreciated a century ago, but only in the last 20 years have we begun to understand how the hemoglobin molecule works. Protein chemists and X-ray crystallographers have established the structure of hemoglobin and have found remarkable structural differences between oxygen-loaded and oxygen-emptied hemoglobin.

Figure 21. *This is a diagrammatic representation of a hemoglobin molecule. The molecule is composed of four chains of amino acids. Each chain encompasses a heme group, shown as a plate, in the center of which is an iron atom, shown as a ball.*



Two decades of rapidly accumulating knowledge of the chemistry of hemoglobin have provided insights into hemoglobin disorders. In sickle cell anemia, for example, we now know the site of a hemoglobin defect that causes the normally round red blood cells to take on the distorted shape of a sickle; this knowledge may lead to pharmacologic treatment of that disease. In diabetes, we have discovered that a higher-than-normal proportion of hemoglobin carries sugar molecules; this may be an important clue for determining effects of the high blood sugar of diabetes on other tissues.

What usually causes defective production of red blood cells?

Nutritional deficiencies are probably the most common cause of defective production, but heredity may also play a part. Iron is an integral part of hemoglobin, and well over half the total iron in the body is normally found in the circulating hemoglobin. Thus even a small chronic daily loss of blood may soon result in iron-deficiency anemia. Nutritional anemias may also result from lack of iron, vitamin B_{12}, or folic acid, all of which are needed for production of normal blood cells.

Have advances been made in understanding hereditary anemias?

Yes. Most hereditary anemias are characterized by an abnormally short life span of the red cells. In addition, the actual cell production may be defective.

Sickle cell disease is a good illustration of a hereditary anemia. An extremely important landmark in our understanding of this disease was the discovery by Linus Pauling and his associates, in 1949, that an abnormal hemoglobin is responsible for sickle cell anemia. When this hemoglobin, now called hemoglobin S, loses its load of oxygen, hemoglobin S molecules aggregate, and the red cells then assume a sickle shape (see figure 22). These misshapen cells clump together and have difficulty in passing through small blood vessels. Sickled cells thus cause occlusion of small blood vessels and are themselves destroyed.

Are there effective treatments for hereditary anemias?

Not yet—and the search for specific treatments is a goal of current research. At present, physicians are concentrating their efforts largely on prevention and management of complications. For example, a common cause of disability and death in young children with sickle cell disease has been found to be pneumococcal infections. A vaccine against the pneumococcus is now available; but in the group at highest risk—under the age of 2 years—its effectiveness remains to be established. Survival and quality of life of patients with sickle cell disease appear to have improved with prompt treatment of infections and attention to high fluid intake, particularly during infections.

Another hereditary anemia is thalassemia (Cooley's anemia). Recent advances in basic research that constitute an exciting chapter in molecular biology have contributed significantly to better understanding and treatment of thalassemia. Indeed, defects in the genes responsible for the manufacture of hemoglobin have been found in the red cells of patients with thalassemia.

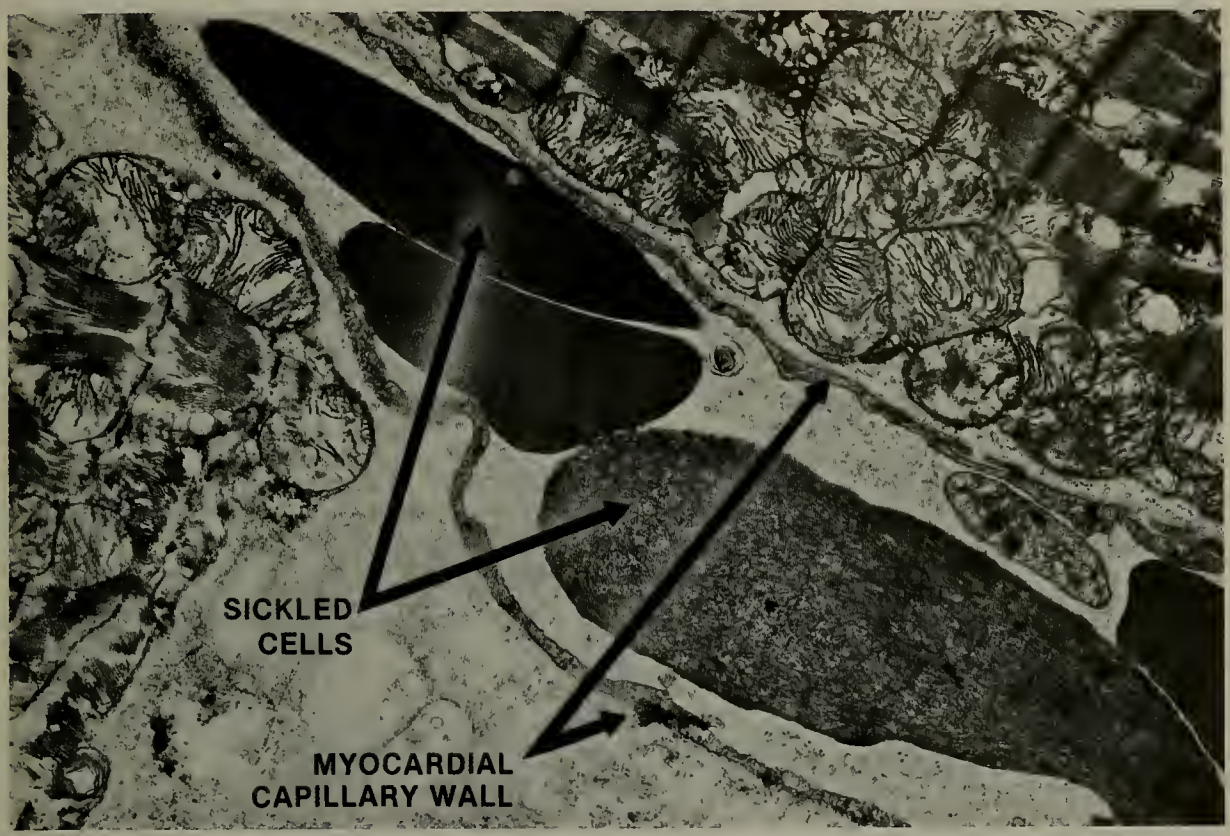
One of the problems of patients with severe thalassemia (and other severe anemias), who require frequent transfusions of red blood cells, is iron overload resulting from the accumulation of iron in the body from repeated transfusions. During the past 4 years better methods of handling this problem have been developed, including treatment with chelating agents that bind iron and promote its excretion from the body. Children with severe thalassemia are now benefiting from improved blood transfusion technology and, it is hoped, from the newer methods of reducing iron overload.

In both sickle cell anemia and thalassemia, important clinical research is now being done on the natural history of the diseases and on evaluation of different kinds of treatment and complications. Recent advances in understanding the causes of thalassemia have not yet found expression in specific therapy, but basic research continues to expand our knowledge of this and other genetic disorders.

BLOOD RESOURCES

BLOODLETTING is centuries old, and transfusions of unmatched blood were given 100 years ago. Although transfusions of matched blood have been given for 40 or 50 years, methodology has changed enormously in that time.

Figure 22. *This transmission electron micrograph shows abnormal sickle-shaped red blood cells blocking a small blood vessel, or capillary, in the heart (magnification x 10,000). For comparison, the appearance of a normal circle-shaped red blood cell can be seen in figure 19.*



Modern medicine would be impossible without modern transfusion technology. In fact, so many procedures depend on the availability of an adequate supply of human blood for transfusions that we sometimes forget the role of transfusions in the evolution of medical and surgical treatment. Surgical procedures such as open-heart surgery would hardly be possible without an adequate and safe supply of blood. Traumatic events that at one time would have been fatal are no longer so because lifesaving blood is rapidly administered.

Forty years ago blood transfusions were available in only a few places. Today transfusion is a routine medical procedure at every medical facility and on the battlefield. Compatibility testing (blood typing) has been greatly improved, making sophisticated testing possible as a routine procedure in blood banks and contributing to the safety of blood transfusion. In addition, detection of hepatitis, which may be transmitted through transfusion, has greatly improved and has already led virtually to the elimination of hepatitis B, formerly the leading type of post-transfusion hepatitis.

In some diseases, such as hemophilia and thalassemia, transfusion of blood or blood components constitutes a major part of therapy. For patients who have experienced temporary suppression of platelet formation as a result of such treatments as radiotherapy or chemotherapy for leukemia, the availability of platelet transfusions represents a major advance in modern-day medicine. Administration of white cells from human blood is now being carried out for infections in patients whose own white cells are inadequate. Red blood cells are given most commonly for many different kinds of anemia. These are only a few of the situations where the administration of blood components constitutes direct and specific therapy.

Figure 23. *Blood transfusions were given over 100 years ago, and the picture below depicts an early blood transfusion of unmatched blood performed at the Hôpital de la Pitié in Paris in 1874. Blood transfusions of matched blood saved many lives during the 1944 Normandy Invasion in World War II (top, facing page). Modern-day blood donations (bottom, facing page) can involve a procedure called pheresis, which selectively collects a single blood component. By this process, whole blood is drawn, the single component is separated, and the remainder of the blood is returned to the donor. Because pheresis removes only one blood component, donors can contribute more frequently than they could if they were donating whole blood. Present pheresis techniques extract plasma (plasmapheresis), platelets (plateletpheresis), or white cells (leukopheresis).*

Have there been many changes in the storage and handling of blood?

A great many changes have occurred. In the 1940's, blood was commonly used in two components—the corpuscular material and the plasma. It was stored in easily breakable and hard-to-handle glass bottles. Today blood is fractionated into components (red cells, platelets, plasma, gamma globulin, antihemophilic factor, etc.), which can be transported readily in plastic containers (see figure 24).

Is an adequate supply of safe blood and blood products readily available today?

Not completely, although we are close to achieving this important goal. Over the past 30 to 40 years, a number of public and private organizations have been involved in collecting, processing, storing, and distributing blood and blood products. The storage of red cells can now be extended from 21 days to 35 days through the addition of a substance called adenine. Furthermore, special but expensive processes of blood freezing provide reserve supplies of blood for unusual circumstances (e.g., very rare blood groups).

With respect to the national blood resource as a whole, no organized, comprehensive approach has been utilized. During the past several years, the American Blood Commission has been organized as a voluntary effort to remedy this situation. Its primary mission is to aid in coordinating blood collection, processing, and distribution. The NHLBI has taken a major interest in this effort and has provided strong support to assist in establishing an efficient nationwide and perhaps worldwide network of blood resource centers.

Are there important areas in which opportunities exist for research in blood resources?

In blood resources, the goal continues to be a fully integrated system of collection and distribution of blood and blood derivatives from volunteer donors, so that safe blood and blood components can be immediately available wherever and whenever needed. These are not problems of biomedical research, but rather of systems development and management, with major responsibility in the private sector.

In biomedical research there are many areas where important continuing development is essential. Blood component therapy has made remarkable advances in the last several years, but in some instances it is expensive, incomplete, and not always effective. For the treatment of hemophilia, for example, better and less expensive antihemophilic factor substitutes are needed. Other forms of component therapy require the development of new fundamental knowledge. A most important and promising approach has been research directed toward the development of both natural and artificial blood substitutes. These fall into two classes: plasma expanders, such as albumin, dextran, and others; and materials capable of carrying oxygen, such as hemoglobin solutions and synthetic fluorocarbons. The development of such substitutes may have a major impact on the national blood resource.

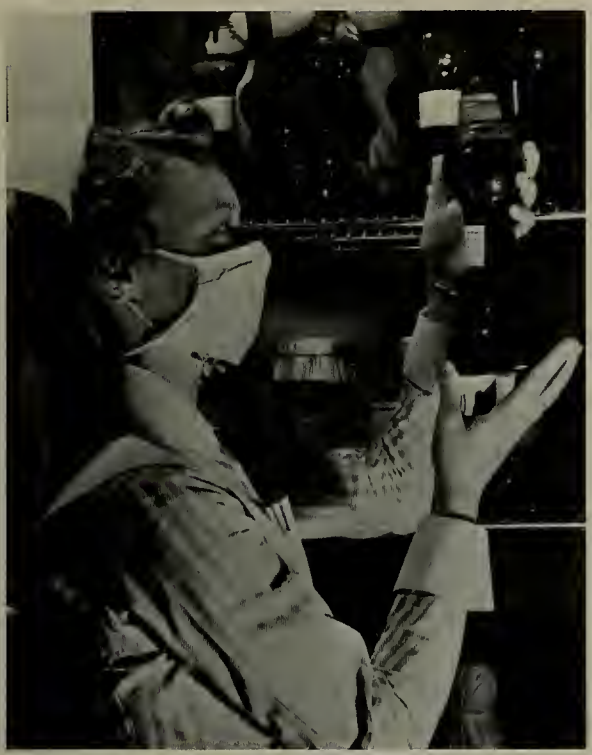


Figure 24. *During the last 30 years, the way in which blood is handled and stored has become more sophisticated. The picture on the upper left was taken in 1940 and shows a nurse handling stored whole blood in easily broken glass bottles. Today, blood is separated into different fractions by whirling in a centrifuge (upper right). This process drives the red and white corpuscles to the bottom of the bottle, after which the clear plasma is drawn off the top. The plasma can be further processed into dried, flaky powder which is used for emergency transfusions. The picture on the left shows blood components stored in plastic containers being shipped to fill emergency needs.*

THE GOAL IS PREVENTION

THE Council is concerned that prevention be emphasized maximally, and for this reason has chosen to use tuberculosis, once one of the most dreaded lung diseases, to illustrate that knowledge of the cause and cure of a disease does not necessarily mean that the disease will be eliminated. Unfortunately, there is a widespread illusion that tuberculosis has been conquered. A cure was discovered in 1948, and tuberculosis is now under control in many countries. However, in many places it is still alive and virulent. It is far from eradicated and remains potentially a great killer.

If we have an effective cure for a disease and the disease has been under control for many years, why can we not eradicate it completely?

There is a difference between control and conquest. To *control* a disease, we usually need to know both the cause and the cure. To *conquer* or eliminate a disease, we also need a way to *prevent* it, just as we now can prevent polio and smallpox with vaccines. The complete conquest of a disease requires all three—determining the cause, finding a cure, and developing the means for prevention. For tuberculosis we have the cause and the cure, but we have no specific means of prevention.

How long did it take to gain control of tuberculosis?

Thousands of years. A mummified body in Heidelberg, Germany, with a tuberculosis-like lesion of the spine, has been carbon-dated back at least 6,000 years. The ancient Egyptians knew about tuberculosis and apparently even had sanatoriums for afflicted persons. Over 1,500 years ago, the French King Clovis decided his touch could cure tuberculosis. The disease thus became known as "the king's evil," which the king's touch would cure. English kings claimed the same power a thousand years later, and on one occasion in 1684 many people with tuberculosis were trampled to death in crowds struggling to get near enough to be touched by the king. John Bunyan in "The Life and Death of Mr. Badman" (1680) described tuberculosis as "the Captain of the Men of Death."

When was tuberculosis first realized to be infectious and contagious?

In 1882—less than a century ago—when Koch discovered that tuberculosis was caused by the tubercle bacillus. That was an enormous advance, but it took another 66 years to find a safe and effective cure in streptomycin. Later came other drugs, and today the disease is under control in much of the world.

Why isn't it under control everywhere?

In this country we have largely eliminated tuberculosis, except in urban ghettoes, Indian reservations, and isolated pockets of poverty. Throughout the world, tuberculosis still exists in areas that share the common factors of poverty, overcrowding, and poor housing, nutrition, and medical care. For this reason, tuberculosis research continues worldwide. In the United States, many agencies and organizations cooperate in this research.

If the cause is known, and curative drugs are available, why is so much research still needed?

Research is needed to find a means for prevention. Maintenance of good health requires prevention of disease; this is our long-term goal for all major diseases. For tuberculosis, continued research has already provided drugs to protect people who have just been exposed. We must continue to aim for a vaccine or other preventive measures. We also need a method for detecting active tuberculosis earlier, and a feasible program for locating the tubercular contact for every new case reported.

It seems as if tuberculosis has not *really* been solved even in affluent countries.

No, not even in our own affluent country. For prevention to be complete, tuberculosis must be totally eradicated, just as smallpox has been essentially eliminated.

For *every* serious disease, *the ultimate goal is prevention*—and this objective will provide fruitful research opportunities for a long time to come. Although research on tuberculosis is not primarily a function of the NHLBI, this example best illustrates the historical importance and complexity of research dedicated to the prevention of disease.

DEMONSTRATION–EDUCATION, PREVENTION, AND CONTROL

THE National Heart, Lung, and Blood Advisory Council has addressed previously in considerable detail the importance of translating biomedical research developments rapidly into health care for treatment and prevention. Progress made in recent years was emphasized in both the 1976 and 1977 reports of the Council, and the many stages in translating basic research into medical care and health care applications were outlined.

Focusing on education, prevention, and control, the Council reiterates its commitment to programs of demonstration with the ultimate goal of increasing the public benefit from biomedical research.

DEMONSTRATION

FOR many years the primary mission of the NHLBI was basic biomedical research. Major research contributions resulted from this commitment, and these advances were brought forward through the traditional channels of dissemination to the public—mainly through medical literature and professional meetings. However, this process had serious shortcomings, for it subjected contributions and observations to the intellectual filtering process that is inherent in these traditional channels. This meant that ideas, observations, and concepts that might be considered ready for clinical investigation or even clinical application would probably not be recognized by physician investigators and practitioners unless they were in accordance with their own interests, needs, and priorities. In short, the traditional communication channels for important biomedical research findings and developments did not assure their translation into improvements in health care. In 1948, when the National Heart Institute was established, there was no effective organized and systematic approach for attaining this objective, and communication and interaction between scientists, health professionals, and the public were not yet major goals of the Institute. Today, such communication and interaction *are* major goals.

Recognition of this need for improved communication, however, is not new. As the Institute's mission has expanded, so has this aspect of its work. By specific mandate of Congress, and especially during the past 10 years, the Institute has undertaken a number of demonstration activities. These have involved the interactions of all of the groups mentioned above in joint efforts to determine better ways of applying laboratory and clinical research to medical care.

The concept of direct communication between basic research programs and demonstration programs, thus bridging the gap between applied research and demonstration, clinical investigation, and clinical trials, as well as ensuring some form of demonstration at the community level, is currently being investigated through NHLBI's Research and Demonstration Centers. The National Heart, Blood Vessel, Lung, and Blood Act of 1972 called for the establishment of Research and Demonstration Centers in heart, lung, and blood diseases, and blood resources. Funding was committed to permit establishment of one center in each of these three major areas. These centers have recently completed their third year of existence, and detailed progress reports are being prepared as part of the Institute's evaluation of the center program. The Council will be prepared to report on this program in greater detail at a later date; the Council's limited observations thus far suggest that important new avenues of communication can be developed in this fashion, and that improved health and medical care will result. Clearly, demonstration at the community level in some form is essential to create links between the biomedical research community, the local health care and medical care providers, and the public. The ultimate goal is to serve the public interest.

EDUCATION

PROGRAMS in education are critically important as part of the translation process. Such programs not only must be designed for patient benefit, but also must provide for the broader needs of public education, including continuing education for health care professionals.

In previous reports, the Council has noted with concern the need to improve continuing medical education programs for physicians. Professional meetings have not provided an adequate means of communication between the laboratory scientist and the practicing physician. The Council is convinced that better means of continuing medical education must be developed, and is even more committed to the concept of an integrated systems approach to maintain

and expand the knowledge of all health care providers. It seems highly desirable to accomplish this in some joint fashion.

The Congress has become increasingly aware of the importance of patient and public education, as evidenced in recent legislation and new legislative proposals. The concept of public education programs in community health centers is being explored by many concerned groups. The Institute has been vigorous in its support of these activities through such programs as the Lipid Research Clinics, the National High Blood Pressure Education Program, and the Comprehensive Sickle Cell Centers, to name a few.

The same Congressional concern was reflected in 1972 by a mandate to the Institute to "disseminate information pertaining to diet." Since then the Institute has:

- Conducted behavioral research studies to learn more effective ways to disseminate nutritional information, as well as to help people achieve and maintain more healthful living patterns;
- Gathered the best available consensus of dietary information, focusing especially on the relation between diet and disease, particularly cardiovascular disease; and
- Enlisted private industry's help in a research and evaluation experiment to determine the most effective way to bring good nutritional information and education to public attention.

This effort has now produced three pilot programs, developed in collaboration with the supermarket, cafeteria, and vending-machine industries. The programs' purpose is to gain attention from the food-buying public at the moment of purchase.

All three programs are now being launched in selected geographic areas. The supermarket experiment is now underway. The cafeteria pilot program is now completed and plans for national dissemination are underway. The vending-machine pilot program will be enlarged to a national effort in conjunction with the National Automated Merchandising Association.

If the pilot programs succeed in disseminating nutritional information in such a way that people understand and apply the information in their daily lives, the Institute will then encourage the adoption of these pilot programs by the food preparation, processing, and retailing industries.

In connection with the need for better public education in medical care problems, perhaps the single most important observation is that the disease and care concepts typically conveyed by health care providers are not necessarily understood by individuals with medical problems. Indeed, patient understanding of the problem is often alarmingly poor, which results all too often in unsatisfactory outcomes. Clearer communication is essential to effect the behavioral changes in the provider, patient, and public that are necessary if our nation is ever to move

Figure 25. *This is one of the cartoons used in the Institute's Nutritional Information and Education Program.*

significantly toward health maintenance and disease prevention. The Council strongly supports the new initiatives in behavioral science that have been undertaken by the Institute to determine more effective means for improving the translation process through patient, public, and continuing professional education.

PREVENTION

PREVENTION refers to action taken before the onset of a disease or the appearance of overt symptoms. The potential value of disease prevention has long been accepted by scientists, health care providers, and the public, for prevention is obviously the only possible alternative to such situations as sudden death from coronary heart disease. The same is true, although less dramatically so, for emphysema, chronic obstructive lung disease, and genetic blood diseases.

Prevention of disease and maintenance of health is an overall mission shared by biomedical scientists, clinical investigators, health care providers, and the public. Goals, objectives, and even priorities of specific groups and individuals are clearly and appropriately different. However, there is growing debate on the state of the art in prevention, especially in terms of dollar costs, the need for medical and allied health personnel, and provision of other health care resources. Nonetheless, there is clearly a strong and growing recognition of the need for prevention, as well as a commitment to accomplish this goal despite the difficulties that are evident.

The principal barrier to prevention in many instances is the lack of adequate scientific knowledge on which to base preventive measures. In other situations where adequate knowledge is available, the problem may be to persuade those most in need to avail themselves of preventive medical services. Some progress has been made in educating people about healthful versus harmful habits and lifestyles, but we have much to learn about how to motivate people to give up bad habits and to adopt good ones. Scientific research, clinical investigation, clinical trials, demonstration programs, and critical evaluation of integrated investigational efforts are needed at the community level to determine the why, when, and how of preventive medicine.

The enormity of the problem should not deter or overwhelm us, for the potential benefits are comparable in size and importance. Thus, in the ideal medical management of a specific disease problem, we first identify the causes of health care problems to remove or modify them and prevent the disease. However, in the history of public health there have been many instances in which successful preventive measures were effected before the cause of a disease was fully or precisely known. Prevention of smallpox, control of cholera epidemics, and prevention of scurvy and pellagra preceded identification of their causes and understanding of their pathogenesis.

The NHLBI has long been committed to disease prevention and health maintenance. For many years the principal thrust to accomplish this mission has been through basic biomedical research and clinical investigations. In atherosclerosis, progress toward prevention can, and in fact has, been made in a number of different ways. The underlying purpose of much research is to detect the basic defect and the steps in the complex pathogenic process that result in clinical complications. The goal of epidemiologic studies is to determine causes, precursors, and risk factors to identify persons who are at risk and to reduce the probability of their dying or suffering from serious illness—in this instance, by encouraging them to stop smoking, change their eating and exercise habits, and adhere to medical treatment to lower their blood pressure.

In recent years, substantial progress toward prevention of mortality from coronary heart disease has come as a result of interrelated activities in several areas: first, persons at increased risk of developing clinical complications can be identified with greater certainty as a result of simple procedures now widely available through physicians' offices; second, clinical trials have been started to assess the feasibility and effect of modifying risk factors; third, the heart attack problem has been confronted at a community level by public education programs sponsored by government, volunteer health agencies, and private groups; and fourth, improvements in clinical management have led to a reduction in death rates among those suffering heart attacks and surviving long enough to receive hospital care. In the last instance, secondary prevention becomes of equal, if not greater, significance.

The Council agrees with the directions and motivations of the Administration and the Congress, as expressed through recent legislative initiatives that support the establishment of a comprehensive disease prevention and health promotion program in the United States. The Institute will certainly continue to expand its efforts and activities in disease prevention.

CONTROL

THE National High Blood Pressure Education Program (NHBPEP) was launched in June 1972. It is the first community disease control program that the NHLBI has undertaken and the first truly national effort to fight hypertension. The program has been highly effective and widely praised for its favorable impact on health care, and especially for its evident contribution to a steep decline in death rates from heart attack and stroke during the past 6 years.

Hypertension (commonly called high blood pressure) is an insidious killer and the most common chronic medical problem seen by physicians. More than 35 million Americans—one in every six—have hypertension requiring some form of treatment to prevent future catastrophic complications. Another 25 million have borderline high blood pressure warranting regular medical surveillance.

Untreated hypertension is the largest single contributor to stroke, and a major contributor to heart disease, heart attack, heart and kidney failure, and other complications. A majority of hospital admissions result from these complications. Long-term epidemiologic studies funded by the Institute (such as the Framingham, Massachusetts, Heart Study) show that in every age group, as blood pressure increases the death rate rises sharply.

Fortunately, hypertension differs from many other chronic diseases in one critical respect. Recent research, especially since 1950, has discovered many safe and effective antihypertensive drugs. Institute-supported clinical trials have proved that these drugs can normalize high blood pressure and prevent its complications in most people. And clinical experience has demonstrated a striking reduction in the frequency of heart and kidney failure and stroke in hypertensive people whose blood pressure is lowered and maintained at normal levels.

Studies and experience have shown that elevated blood pressure can also be lowered to some extent by reducing dietary intake of sodium (salt), reducing weight, exercising adequately, and not smoking cigarettes. Thus the combination of antihypertensive drug treatment, dietary improvement, and other lifestyle changes can control high blood pressure and provide reasonable assurance of a normal life span for most people with hypertension.

Unfortunately, however, medical attention to hypertension usually begins much too late. The disease starts stealthily, often early in life, without any warning symptoms. The victim may feel fine all of the time that high blood pressure is causing damage throughout the body. This damage takes place in complete silence for many years before suddenly appearing in some complication—often an event as disastrous as heart attack, stroke, kidney failure, or even sudden death.

This explains why hypertension is known as "the silent killer." It also explains why studies in the early 1970's showed that *half of all Americans with high blood pressure did not know they had it, over half of those who did know were not on effective treatment, and less than one-eighth of the population with hypertension were on effective blood pressure control.*

These findings prompted the Institute to launch the National High Blood Pressure Education Program, which was directed at both health professionals and the public. The goals of the program were to: (a) stimulate a national mobilization of people and resources to create community hypertension control programs everywhere possible; (b) educate physicians and other health professionals in the latest knowledge of nutritional and drug treatment of hypertension, and motivate their support of and active participation in local detection and referral programs; (c) educate the public about the seriousness of high blood pressure and the importance of treatment; and (d) most importantly, encourage as many untreated hypertensives as possible to visit their physicians for evaluation and treatment.

Since 1972, the program has helped to identify millions of untreated and previously undetected hypertensives. More than 10 million Americans are

Figure 26. *On the left, this woman's blood pressure is being measured as part of a community detection effort of the National High Blood Pressure Education Program. Participants receive assistance in obtaining care should this be necessary.*

On the right, this teenager is having her blood pressure followed closely, since hypertension poses a special threat to the black community. This is part of the Bogalusa Heart Study to determine what factors cause hypertension in youngsters and how these factors change when children become adults with heart disease.

now under effective blood pressure control, compared with 3 million at the start of the program. During this same period, according to data compiled by the National Center for Health Statistics, the death rate from stroke has fallen by over 20 percent and that from heart attack by over 15 percent. Although cardiovascular mortality had been declining gradually from 1950 to 1972, a steep drop has occurred during the 6 years of the National High Blood Pressure Education Program.

To pursue this broad national effort, the Institute serves as the principal leadership agency, working with many other agencies and groups, both private and public. To develop an approach, the Institute joined with volunteer health agencies, industry, professional organizations, civic and consumer groups, concerned lay individuals, a variety of other resource groups, and representatives of the news media.

At the community level, detection and referral of persons with high blood pressure has been carried on by thousands of local leaders and civic groups specially mobilized for these purposes. Countless health professionals have contributed time and skills to these endeavors; they include physicians, nurses, dentists, pharmacists, optometrists, podiatrists, health educators, community outreach workers, and many others.

A High Blood Pressure Coordinating Committee is responsible for liaison among the many cooperating organizations. Organizations represented on this committee include the American Academy of Family Physicians, American College of Cardiology, American Heart Association, American Hospital Association, American Nurses Association, American Osteopathic Association, Citizens for the Treatment of High Blood Pressure, National Medical Association, National Kidney Foundation, and many others.

Figure 27. *Accurate measurement of blood pressure in very young children is facilitated by the special equipment shown. A highly trained paramedical worker places a small cuff with a tiny instrument which emits high frequency sound waves on the child's arm. The echoes from these sound waves reveal the pressure in the blood vessels underneath.*

Many important educational and operational developments have resulted from this program and have, in turn, contributed to its effectiveness. Some highlights include:

- *Guidelines for the Detection, Evaluation, and Management of High Blood Pressure* have been developed and published for health care professionals.
- A yearly National Conference on High Blood Pressure Control now attracts broad representation from lay and professional groups interested in community disease control programs.
- High blood pressure education guidelines and approaches have been established for the public, the patient, and as part of undergraduate, graduate, and continuing medical education for health care professionals.

The favorable results of the National High Blood Pressure Education Program have extended the program's influence far beyond its immediate effect of improving the health care of the millions of people afflicted by hypertension. The program has demonstrated the merit of pooling public and private talents, energies, and resources in a massive, concerted action against a particular public health problem. This experience may serve as a model that can be adapted to similar mobilizations against other common medical and health care problems.

The NHLBI is committed not only to continuing the National High Blood Pressure Education Program, but also to determining step-by-step how this experience can be practically applied in the management of other health care problems. The Council strongly supports continuation of this leadership role by the Institute.

RESEARCH MANPOWER TRAINING

IN no other field of endeavor is the prepared mind more crucial than in biomedical research. The Council believes that the best research is likely to be done by hands and minds that have been trained specifically for research, and that a stable and effective research manpower training program is an essential component of a long-range plan to advance the attack on heart, blood vessel, lung, and blood diseases. The Council believes that it is urgent to develop a plan for at least 5 years and preferably for 10.

In 1969, the NHLBI's mission was broadened considerably by the addition of primary responsibility for thoracic and pulmonary diseases. The mandate of the Institute was further enlarged in 1972 and 1976, with a greater emphasis on blood diseases and blood resources. Despite the much greater responsibility and the need to commit resources to support research in lung and blood diseases and blood resources, funding of the Institute has not been increased consistent with the mission. This is also true with respect to the support of manpower training programs.

In 1972, the Institute provided stipends for research training for 675 full-time and 670 part-time research fellows or trainees. In 1973, the Administration moved to phase out research traineeships. More recently, there has been strong support for research manpower training programs. However, support of these programs is still subject to considerable fluctuation, and debate continues on how many and what type of researchers should be trained.

The Council is especially troubled by the decline in the number of physicians who receive research training support through the Institute. This number declined from 384 in FY 1976 to 307 in FY 1977, and preliminary data suggest it will decline even further in FY 1978. The reduction in physician manpower training is reflected not only in fellowships, but also in the declining number of physicians who receive Research Career Development Award (RCDA) support. During FY 1978, only 38 percent of active RCDA's supported by the Institute's Division of Heart and Vascular Diseases had the M.D. degree; others had doctorates in nonclinical sciences.

The Council recognizes that a variety of factors influence the level of support for manpower training. Further, the Council is aware of the current debate on national needs and priorities. The Council vigorously supports those who give a very high priority to the training of new investigators, particularly physicians who desire careers in clinical investigation.

The training programs supported by the NHLBI have performed creditably despite problems in achieving a stable support base. The manpower training program in lung diseases has been especially successful in stimulating new and additional investigators to enter the field. The fruits of training additional biomedical and clinical scientists in the pulmonary field are well demonstrated through the increased number of research applications and other meritorious requests for support monies. Appropriate contributions of new knowledge are increasingly seen in the published literature.

There is reason for concern about the present potential for training new research manpower in the fields of blood diseases and blood resources. The Institute has only recently assumed responsibilities in these areas. Existing research manpower with a major commitment, especially to clinical investigations, is extremely limited. Support for research and research training will present a major problem unless the Institute's current level of funding for these purposes can be augmented.

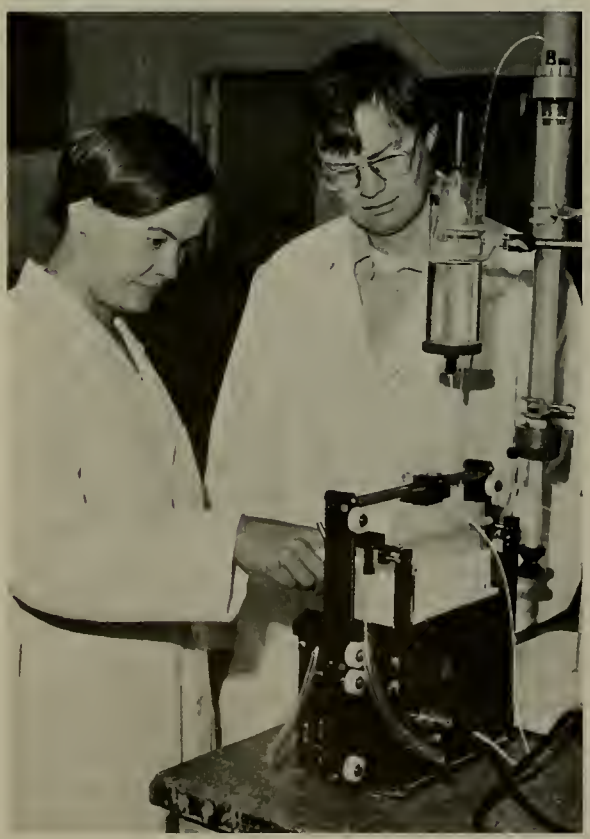
In 1973, the Council's first report to the President and the Congress emphasized the Council's belief that "... the responsibility for training young medical scientists is clearly that of the Federal government and not that of state or local governments. Young scientists are a valuable national resource and their training is a national obligation because their work benefits all of our people in all fifty states." This is still the Council's position, and it is underscored by the fact that the Congress has maintained steadfast support for research manpower training despite the vacillations of past administrations. *The Council strongly endorses the wisdom of this judgment and continues to recommend the principle of Federal responsibility for such training, as advocated in the 1973 report.*

We believe that training opportunities should be provided at both the pre- and postdoctoral levels. Further, training periods should be extended beyond the customary 2 or 3 years in order to assure the young investigator a period of stability long enough

to establish a reasonably competitive level of performance. Regardless of this consideration, support of the trainee beyond the first year in the laboratory should be based on satisfactory performance.

The most critical time in manpower training is probably during the first 3 to 5 years of research experience. It is urgent for young investigators in training to have stable support during this period, in which there is the additional burden of establishing their own laboratories. Outstanding performance during the first and second years of training, and the desire to continue, should be primary determinants of assured research training support for a total of 5 years.

Figure 28. *The veterinarian (left) is explaining laboratory techniques to her student. This training program in comparative hemostasis for postdoctoral students is supported by the NHLBI.*



The Council considers it especially important to emphasize the need for a long-range program of stable support for physician-investigators.

The investigator with the M.D. degree usually has had significantly more experience at the undergraduate and graduate levels before entering biomedical research. One or two years of research experience are often needed to determine the individual's potential and commitment for a research career. The Council will soon bring forward a specific plan for a special-emphasis research fellowship program for M.D. investigators, recognizing that the physician-scientist is indispensable for translating biomedical findings into patient care.

The Council emphatically supports continuation of the Institute's program to encourage minority representation in biomedical research. The Minority Hypertension Research Development Summer Program has been well received. It is anticipated that this program will be continued and its financial support increased. The Minority Biomedical Research Program supported by the NIH Division of Research Resources has also been well received and the Council supports its continuation, as well as continuation of the Minority Access to Research Career Programs sponsored by the National Institute of General Medical Sciences.

RECOMMENDATIONS OF THE NATIONAL HEART, LUNG, AND BLOOD ADVISORY COUNCIL

IN arriving at the recommendations that follow, the Council has taken into account the notable accomplishments of the Institute's program during the past 30 years, the remarkable opportunities for additional progress created by our increasing knowledge of heart, lung, and blood disorders, and the improvement that has already been achieved in mortality rates, especially from cardiovascular diseases.

It is against this perspective that the Council has undertaken to define its recommendations for the Institute's immediate and long-range future. The Council's short-range recommendations are focused on the immediate continuity and momentum of the Institute's leadership role in research in heart, lung, and blood diseases. The long-range recommendations are addressed to the Institute's own resources and requirements during the years ahead.

MANPOWER TRAINING

The single most pressing need in heart, lung, and blood research is for stabilization, improvement, and expansion of the research manpower training programs. The Council is concerned that there is already a shortage of highly skilled researchers in heart, lung, and blood diseases, and that this shortage will become more severe in the decade ahead. This will be especially true with respect to the number of physician-investigators, because the number of such investigators in training has decreased strikingly during the past 5 years.

We strongly urge expansion of the institutional and individual research service awards, the development of new training programs with particular emphasis on the training of physician-investigators, expansion of the programs for young investigators and research career development, and increased availability of support monies for the research programs of young investigators as they begin to establish their own laboratories.

ATHEROSCLEROSIS RESEARCH

Significant advances have been made in establishing a better understanding of atherosclerosis and the complications of the atherosclerotic process, including heart attack and thrombosis. The highest priority should be given to vigorous pursuit and expansion of research programs concerned with thrombosis and atherosclerosis, without delay, because there is good reason to believe that such research will contribute in the near future to further decreases in stroke and heart attack death rates.

SUDDEN DEATH

Heart attack (myocardial infarction) is the single most common cause of death in our country. The long-range goal must be to prevent heart attack; however, the more urgent immediate need is to continue studies of ways to reduce infarct size (thus lessening the severity of the heart attack) and to prevent fatal heart arrhythmias. Expanded support of research programs concerned with sudden death is strongly encouraged.

PATIENT EDUCATION

High blood pressure is one of the major risk factors for myocardial infarction. A long-term goal of research programs is to determine the cause, cure, and prevention of this disorder, which probably afflicts more than 35 million Americans. However, current nutritional and drug therapy programs can achieve control (normalization) of blood pressure in the vast majority of persons with hypertension. The Council therefore feels it most important to effect uninterrupted and increased support of the National High Blood Pressure Education Program. In addition, the beginning initiatives in demonstration and implementation of improved nutrition education deserve high priority for funding and expansion, as do other disease control programs.

PUBLIC EDUCATION

Chronic obstructive lung disease has increased alarmingly in frequency and as a cause of death during the past decade. We strongly encourage expanded and extended basic research, clinical investigations, public and patient education, and control efforts related to the cause, cure, and prevention of chronic obstructive lung disease.

It is most important for the public to benefit directly from more effective initiatives in education. Educational programs should call the attention of all citizens to the extremely harmful consequences of cigarette smoking and should help individual citizens to terminate or avoid use of tobacco.

NUTRITION RESEARCH

Recent investigations have suggested possible protective effects of increased blood levels of high-density lipoproteins and the probable pathogenic significance of high levels of low-density lipoproteins. The Council places a high priority on continued and expanded efforts to achieve a better understanding of the interrelationships between these lipoproteins, the atherosclerotic process, and the incidence of cardiovascular disease and cardiovascular mortality rates. We urge that the Institute vigorously support expanded efforts to determine the role of nutrition in the epidemiology of atherosclerosis through the Lipid Research Clinics and other appropriate vehicles.

NEW TREATMENT

The hereditary anemias continue to be important causes of disability. Important immediate research steps are studies of the events that lead to sickling of red cells, the assessment of pharmacologic agents that impair sickling, and studies of the natural history of sickle cell anemia. The long-range solution of the problems of thalassemia and sickle cell disease may be found through continued research in the genetic mechanisms of hemoglobin disorders; however, more immediate research goals—especially with respect to thalassemia—are assessment of optimal transfusion therapy and of pharmacologic approaches to iron overload.

A SAFE BLOOD SUPPLY

Advances in blood replacement and blood component therapy have contributed in major ways to improved health care and medical care during the past 10 years. It is of extreme importance to continue research to improve the availability of safe blood and blood components. These long-term goals should also include the development of effective blood substitutes. However, of even greater significance in the immediate future is the continued national effort to assure the availability of safe blood and blood products whenever and wherever they are needed. These are major problems that will have to be solved before we may hope to have an adequate substitute for human blood cells.

TECHNOLOGY ADVANCEMENT

Improved technology during the past 30 years has contributed significantly to advances in the medical and surgical treatment of a broad variety of heart, blood vessel, lung, and blood disorders. Prevention of such disorders must remain the long-term goal; however, advances in technology are of great immediate need if we are to expand on the current improvements in reduction of death rates from heart attack, acute respiratory distress syndrome, stroke, kidney failure, and other life-threatening emergencies. Increased Institute support of technology advancement is urged.

DIABETES RESEARCH

Vascular disease associated with diabetes is probably increasing in frequency and severity, and warrants special emphasis on research as to cause, cure, and prevention. The Council commends the Institute's current initiatives in diabetes, and urges it to continue and expand research programs to increase our understanding of this serious disorder.

LONG-RANGE PLANNING

The Council is impressed with the efficient and successful management of the programs of the National Heart, Lung, and Blood Institute afforded by the Director and his staff. Despite major additions to the Institute's overall mission during the past 10 years, corresponding expansion of its facilities, manpower, and funding has not occurred.

The Council is especially concerned with the need for greater centralization and improvement of the Institute's facilities to assure more efficient working relationships among the staff. We strongly recommend that a long-term commitment be made to improve the Institute's facilities and meet its manpower needs in order to better implement its programs.

RESOURCE NEEDS—BUDGET

In recognizing the challenges of accomplishing program balance, the Council faces the responsibility of reassessing the priorities of the NHLBI in order to be realistic with its budget recommendations. Events during 1978 have given both the President and the Congress ample evidence of the prevailing public attitude.

The revised downward trend of this Council's recommendations in no way contradicts the estimates in the *Fifth Report of the National Heart, Lung, and Blood Advisory Council.** We reaffirm the needs for previously stated budget levels.

The fact remains, however, that the necessary dollars may not be available. Therefore we urge latitude in authorization levels, with a firm dedication to a tightened budget belt—but one that will not strangle or jeopardize the responsibility of science to meet the critical demands for continuity of progress. The result of priority reassessment, likewise, does not conflict with the Council's stated purpose. It is solely the expedient of timely necessity.

Measured against the reality of inflation, the recommended increases over the 1979 budget actually represent cost containment, with a substantial reduction from last year's recommendations. These increases constitute the absolute minimum deemed necessary to prevent inflation from undermining the past 30 years' investment in scientific progress of the Institute.

Table 3. *The National Heart, Lung, and Blood Advisory Council's Recommended Annual NHLBI Budget for Fiscal Years 1980-1983.*

Program Activities	Fiscal Years 1980	1981	1982	1983
	(dollars in thousands)			
Extramural Research Programs				
Heart and Vascular Diseases	$295,000	$347,400	$404,400	$473,000
Lung Diseases	76,000	89,500	104,000	121,800
Blood Diseases and Blood Resources	76,000	89,500	104,000	121,700
Prevention, Control, and Education	32,000	35,000	40,000	45,000
Construction	20,000	20,000	20,000	20,000
Manpower	35,000	38,000	43,000	45,000
Intramural Research Programs	43,000	45,000	47,200	50,000
Program Management and Program Services	33,000	35,600	38,400	41,500
TOTAL	**$610,000**	**$700,000**	**$801,000**	**$918,000**

*DHEW Publication No. (NIH) 78-1418.

GLOSSARY

acute – Reaching a crisis rapidly, or having a short and relatively severe course.

acute myocardial infarction – See **heart attack.**

adult respiratory distress syndrome – Recently recognized syndrome of acute and frequently fatal respiratory distress. Occurs in extremely stressful situations accompanied by severe damage to all or part of the body, during or after such events as automobile accidents, surgery, or severe lung infections.

alveoli – Tiny air sacs in the lungs where gas exchange in breathing takes place. Through the thin wall of the alveoli, carbon dioxide in the blood is replaced by fresh oxygen from inhaled air.

anemia – Presence of a subnormal number of red blood cells or of their principal constituent, hemoglobin, of which iron is an essential component.

angina pectoris – Pain in the chest, and often in the left arm and shoulder, typically brought on by exercise or stress, and caused by shortage of oxygen reaching heart muscle. Generally due to atherosclerotic narrowing of the coronary arteries, which supply blood and oxygen to the heart muscle.

arrhythmia – Irregularity or abnormally slow rhythm of the heartbeat. See **pacemaker.**

arteriosclerosis – Hardening of the arteries. Various conditions cause artery walls to thicken, harden, and lose ability to expand and contract. See **atherosclerosis.**

atherosclerosis – Most common and important form of arteriosclerosis, in which the inner layer of the artery wall is made thick and irregular by soft, fatty deposits of cholesterol or other fatty substances. The deposits are known as atheroma or atheromatous plaques. They narrow the diameter of the internal channel of the artery, and may reduce or obstruct (occlude) the flow of blood. When they break loose, they may obstruct the flow of blood elsewhere. See **embolism.**

atherosclerotic plaque –See **atherosclerosis.**

bacterial endocarditis – Inflammation of the inner lining of the heart, caused by bacterial infection and frequently damaging to heart valves. See **cardiomyopathy.**

bronchitis – Inflammation of the bronchial tubes. See **chronic obstructive lung disease.**

cardiac arrhythmia – See **arrhythmia.**

cardiac pacemaker – See **pacemaker.**

cardiomyopathy – A disorder of the heart muscle or valves that may result from various causes, many of which are still unknown or incompletely understood.

cardiopulmonary resuscitation – A nonsurgical lifesaving procedure for cardiac arrest emergencies. Procedure combines rhythmic manual pressure on chest by both hands, with mouth-to-mouth breathing. It can be performed successfully by trained laymen.

cardiovascular – Related to or involving the heart and blood vessels.

cerebral ischemic episode (or **attack**) – Temporary reduction or interruption of blood supply to some part of the brain. Also known as transient ischemic attack. Ischemia is deficiency of blood in some part of the body, caused by constriction or obstruction of a blood vessel. See **stroke.**

cerebral thrombosis – See **stroke.**

chronic – Persisting over a long period of time.

chronic obstructive lung disease – Chronic cough and breathlessness caused by structural damage to alveoli (small air sacs in the lung) and breakdown of self-cleansing system of lungs and airways. Includes basic aspects of both emphysema and chronic bronchitis. The major cause is cigarette smoking. See **cilia.**

cilia – Tiny, hairlike structures on inner walls of airways. Cilia beat rhythmically and thus sweep mucus, bacteria, and other matter upward and outward for removal as sputum.

clinical trial – A controlled study of one or more therapies to determine or compare their effects on a disease process in patients.

coagulation – Clotting of blood.

congenital – Existing at birth, but not necessarily hereditary.

congestive heart failure – Loss of the heart's ability to pump out the blood that returns to it from the veins as quickly as normal. Causes accumulation of abnormal quantities of fluid in body tissues, including those of the lungs.

coronary arteries – Arteries that supply blood and oxygen to the heart muscle. Called "coronary" because they encircle the heart.

coronary artery disease – See **coronary heart disease.**

coronary heart disease – Atherosclerosis of coronary arteries, with narrowing of internal channel and reduction of blood supply to heart muscle. See **atherosclerosis.**

coronary thrombosis – Obstruction of a main coronary artery by a blood clot. See **heart attack.**

diabetes – Metabolic disorder characterized by impaired ability to metabolize carbohydrates, and by damaging effects on all systems of the body, severe complications, and premature death.

echocardiography – Sonarlike noninvasive method of "looking" inside organs and blood vessels without X-ray or surgery.

embolism – Movement of a blood clot (embolus) in the blood stream to a smaller vessel, where it obstructs circulation. See **thrombosis.**

emphysema – A condition of the lung characterized by destruction of thin walls of alveoli. Strongly associated with cigarette smoking. See **chronic obstructive lung disease.**

enzyme – A complex organic substance manufactured by the body, capable of speeding up a specific biochemical process.

fibrillation – Wild, uncoordinated twitching or quivering of individual heart muscle fibers, during which the heart cannot beat properly and pumping action stops. Caused by severe disturbance of the heart's electrical activity.

fibrin – Elastic, insoluble protein that forms a fibrous network for clotting of blood.

gangrene – Death of a mass of body tissue, especially a limb, such as a foot or leg. Usually caused by deprivation of oxygen and nutrition through loss of blood circulation.

heart attack – Rapidly occurring damage or death of an area of the heart muscle (myocardium), caused by reduction or blockage of blood supply. This is usually caused by narrowing or obstruction of one of the two main coronary arteries or their branches, which conduct blood to the heart muscle. The medical term for heart attack is **acute myocardial infarction.**

heart failure – Partial failure of the heart's pumping action to maintain adequate flow of blood to all tissues of the body.

hemoglobin – Oxygen-carrying red pigment of the red blood cells. Iron is an essential component of hemoglobin.

hemolysis – Liberation or separation of hemoglobin from red blood cells. Shortens life span of red cells, causing hemolytic anemia.

hemophilia – Bleeding tendency caused by hereditary deficiency of a specific clotting factor in the blood.

high blood pressure – See **hypertension.**

hypertension – Persistent elevation of blood pressure above the normal range. If untreated, may lead to increased heart size, kidney damage, stroke, heart attack, or other complications. Commonly called **high blood pressure.**

hypertrophy – Enlargement of a tissue or organ. Enlargement of heart may result from increased work caused by hypertension or atherosclerosis.

ischemia – Lack of blood supply in some part of the body, usually temporary, caused by narrowing or obstruction of a blood vessel.

isotope – See **radioactive isotope.**

lesion – An injury or other abnormality in the structure or function of a tissue or other part of the body.

macroangiopathy – Disease of large blood vessels, associated with diabetes.

microangiopathy – Disease of small blood vessels, associated with diabetes.

myocardial infarction – See **heart attack.**

myocarditis – Inflammation of the heart muscle (myocardium).

myopathy – Disease of muscular tissue.

obstructive lung disease – See **chronic obstructive lung disease.**

occlusion – Obstruction of flow in a blood vessel, usually an artery, caused by narrowing of the vessel or the presence of a clot.

pacemaker – A small, implantable electrical device that can correct an irregular or abnormally slow heart rhythm.

plaque – See **atherosclerosis.**

plasma – The cell-free liquid portion of uncoagulated blood.

platelet – Minute circular or oval disk in the blood, involved in clotting.

radioactive isotope – An element that can be used to trace the movement of substances in the body.

respiratory distress syndrome – See **adult respiratory distress syndrome.**

respiratory failure – A condition in which a person is unable to maintain a normal level of oxygen in the blood and lungs. The effect is dizziness, mental confusion, and finally coma.

rheumatic fever – Disease, usually of childhood, that may follow certain streptococcal infections and may cause heart damage, especially valvular. See **rheumatic heart disease.**

rheumatic heart disease – Damage to the heart by attacks of rheumatic fever, particularly scarring of heart valves so that they do not open and close normally. Also involves damage to heart muscle. See **rheumatic fever.**

sickle cell anemia – A hereditary anemia in which the red blood cells assume abnormal, irregular "sickle" shapes when they are deprived of oxygen.

streptococcal infections – See **streptococcus.**

streptococcus – A genus of microorganisms, one species of which (known as beta-hemolytic streptococcus) causes the streptococcal infections that precede rheumatic fever.

stroke – Rapidly occurring damage to brain caused by obstruction or rupture of a blood vessel.

sudden death – Death that occurs extremely rapidly after the onset of symptoms–either instantly, within several minutes, or within 24 hours. Most often related to the heart, and then termed more specifically **sudden cardiac death.**

syndrome – A set of symptoms that occurs together and is therefore given an identifying name.

thalassemia – A group of hereditary anemias characterized by various defects in the manufacture of hemoglobin.

thrombophlebitis – Inflammation and blood-clotting in a vein.

thrombosis – Formation or presence of a blood clot (thrombus) inside a blood vessel or heart cavity, where it may obstruct flow of blood. See **embolism.**

trauma – Wound or injury.

valvular heart disease – Disorder of one or more heart valves, most commonly due to rheumatic heart disease, but sometimes due to other acquired or congenital causes. See **rheumatic heart disease.**

ventricle – One of the two lower chambers of the heart. Term most often used in reference to the *left* ventricle, which serves as the main pump of the heart.

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